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FIG. 1A

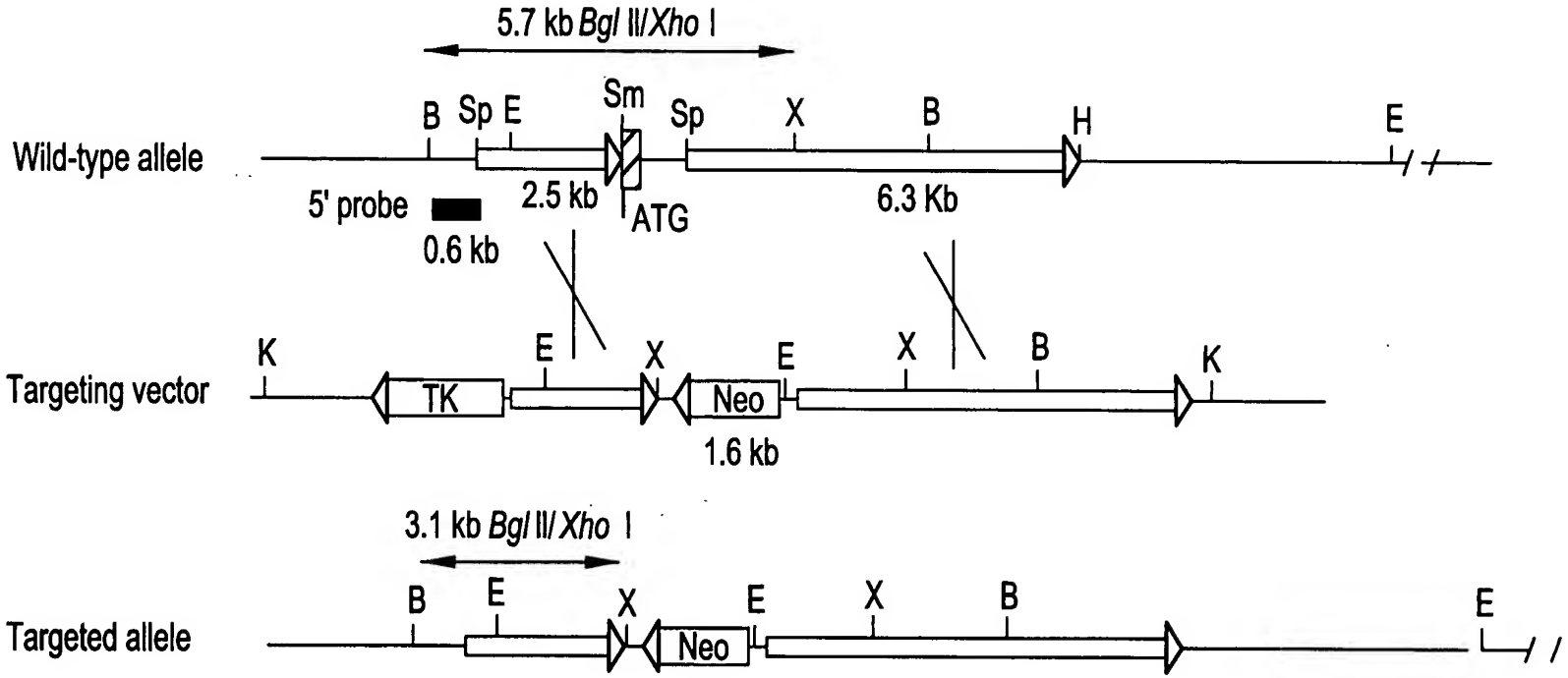

5.7 kb Bgl II/Xho I
Wild-type allele
B
Sp
E
Sm
Sp
X
B
H
E
5' probe
2.5 kb
ATG
6.3 Kb
0.6 kb
Targeting vector
K
E
X
E
X
B
K
TK
Neo
1.6 kb
3.1 kb Bgl II/Xho I
Targeted allele
B
E
X
E
X
B
E
Neo

FIG. 1B

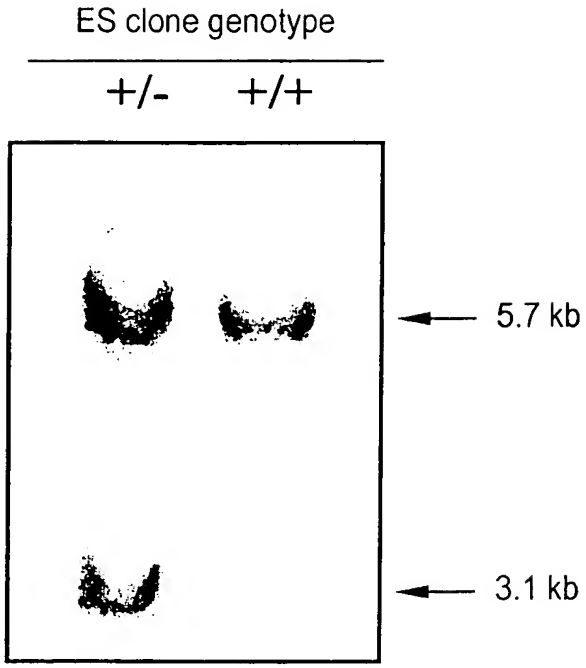


FIG. 1C

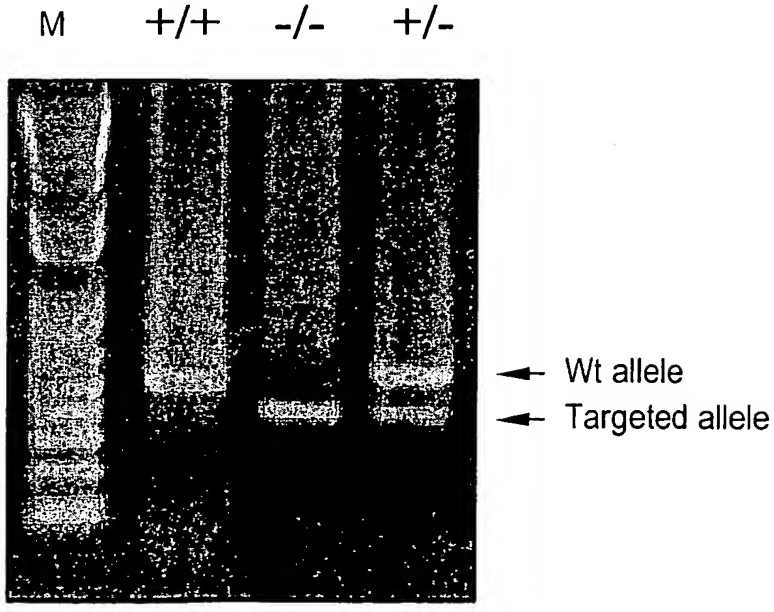


FIG. 1D

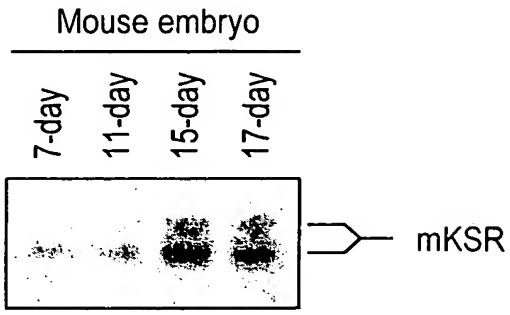


FIG. 1E

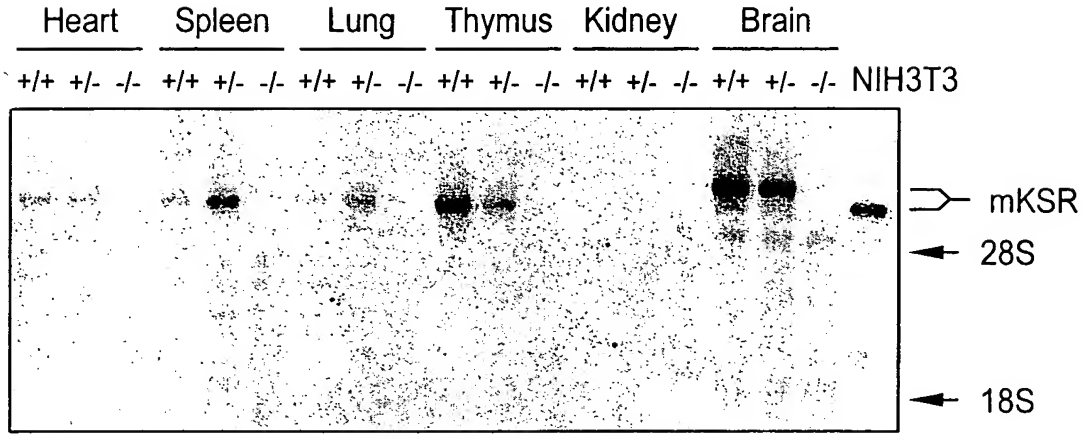


FIG. 1F

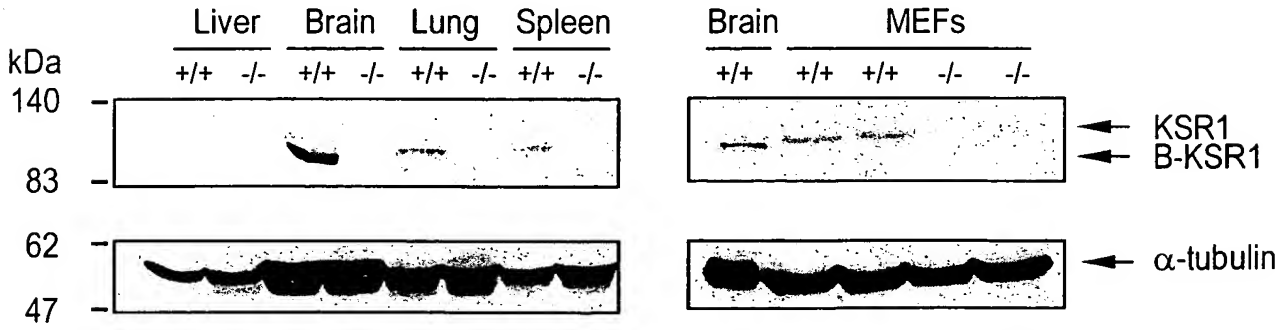


FIG. 2A

a - KSR +/+

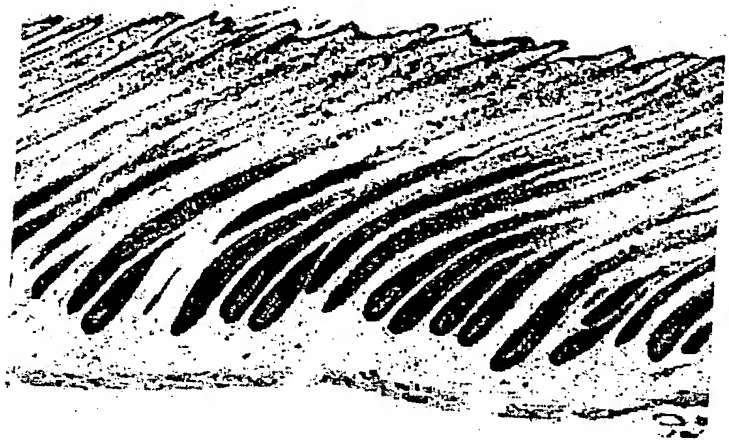


FIG. 2B

b - KSR -/-

FIG. 2C

c - KSR -/-

FIG. 2D

d - EGFR -/-

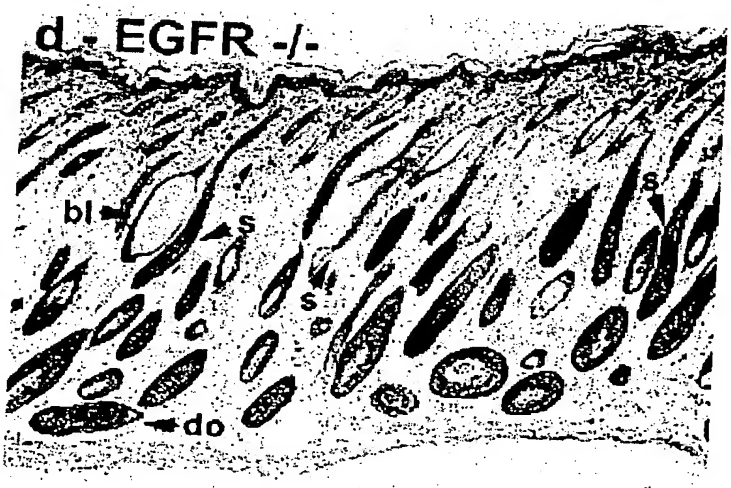


FIG. 3A

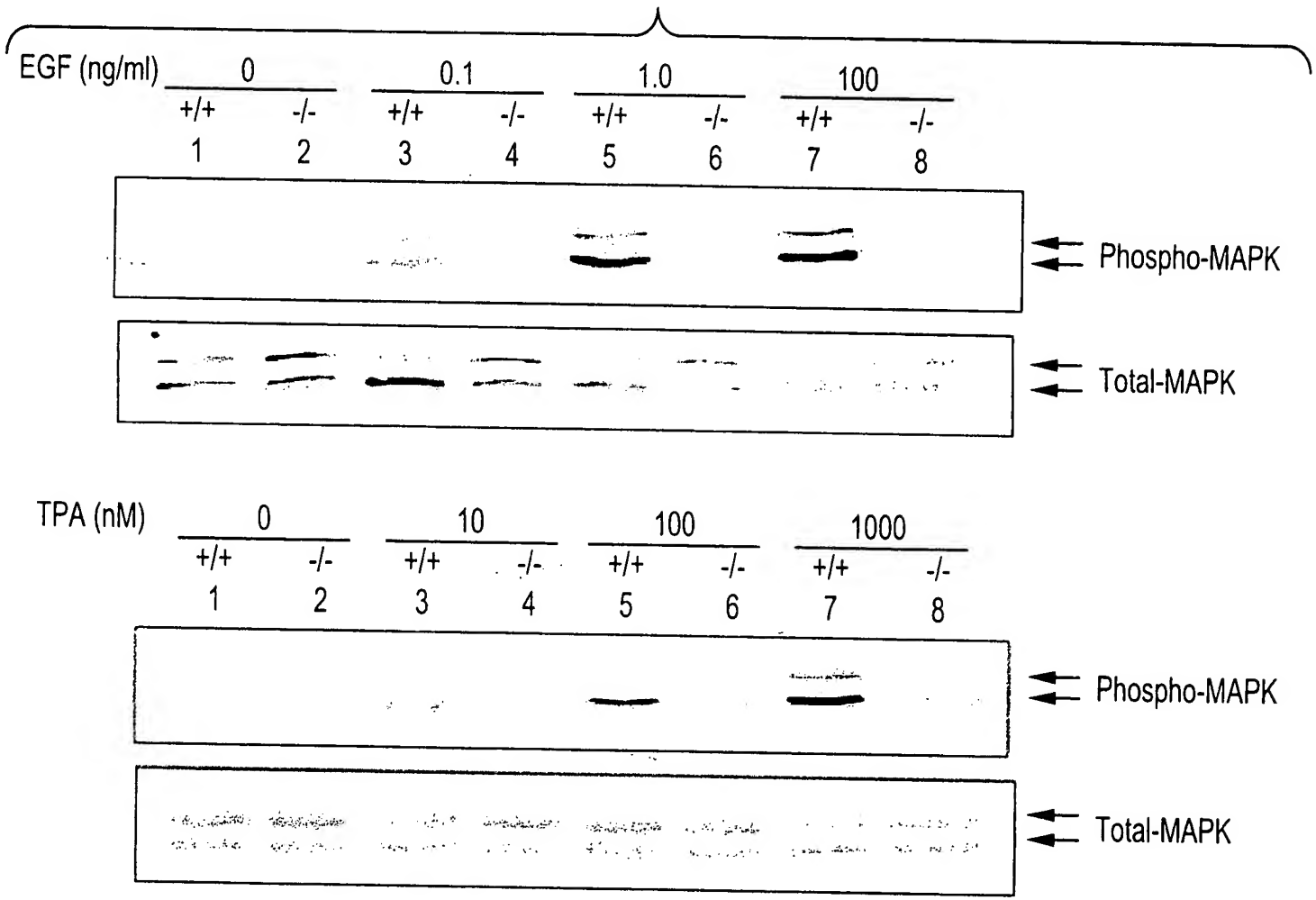

EGF (ng/ml)
0
0.1
1.0
100
+/+
-/-
+/+
-/-
+/+
-/-
+/+
-/-
1
2
3
4
5
6
7
8
Phospho-MAPK
Total-MAPK
TPA (nM)
0
10
100
1000
+/+
-/-
+/+
-/-
+/+
-/-
+/+
-/-
1
2
3
4
5
6
7
8
Phospho-MAPK
Total-MAPK

FIG. 3B

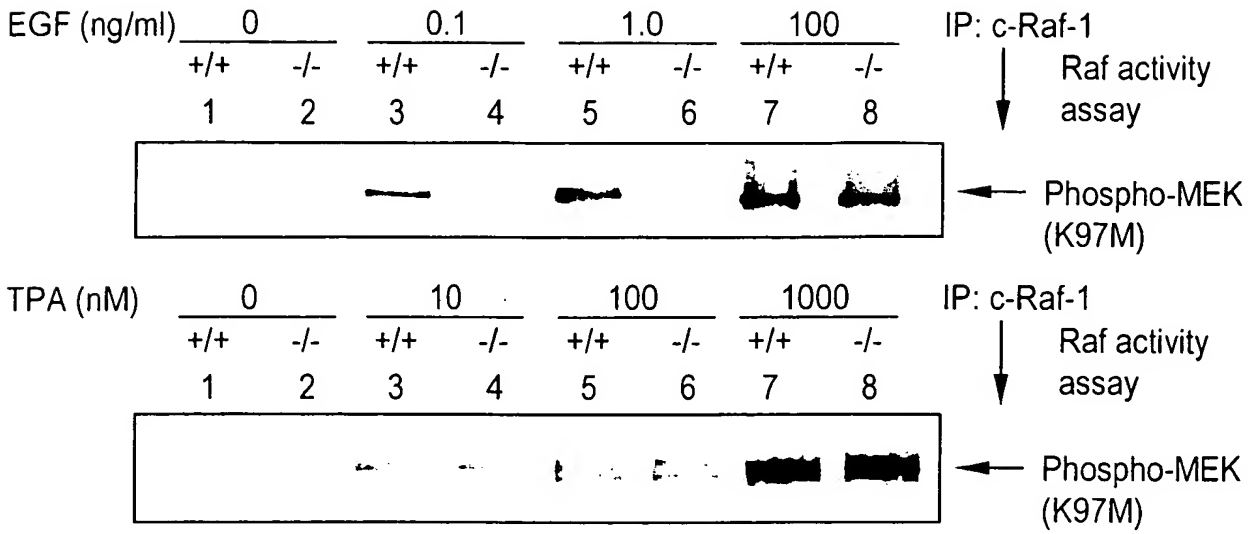

EGF (ng/ml)
0
0.1
1.0
100
+/+
-/-
1
2
3
4
5
6
7
8
IP: c-Raf-1
Raf activity assay
Phospho-MEK (K97M)
TPA (nM)
0
10
100
1000
IP: c-Raf-1
Raf activity assay
Phospho-MEK (K97M)

FIG. 3C

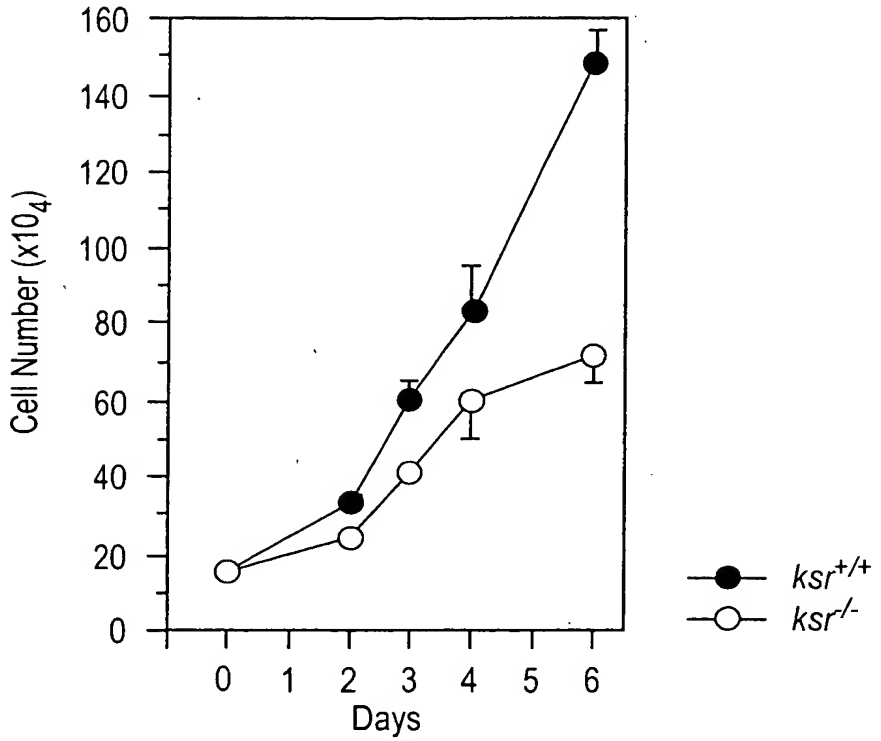

Cell Number (x10$_4$)
160
140
120
100
80
60
40
20
0
0
1
2
3
4
5
6
Days
ksr+/+
ksr-/-

FIG. 4A

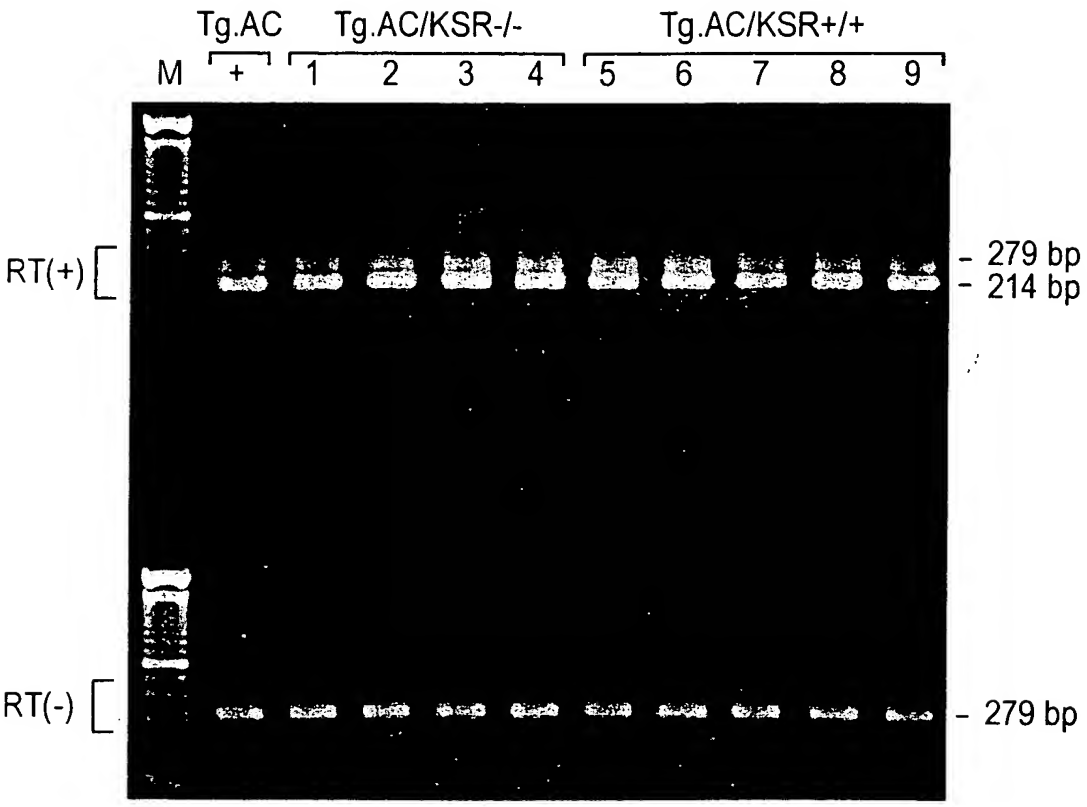


FIG. 4B

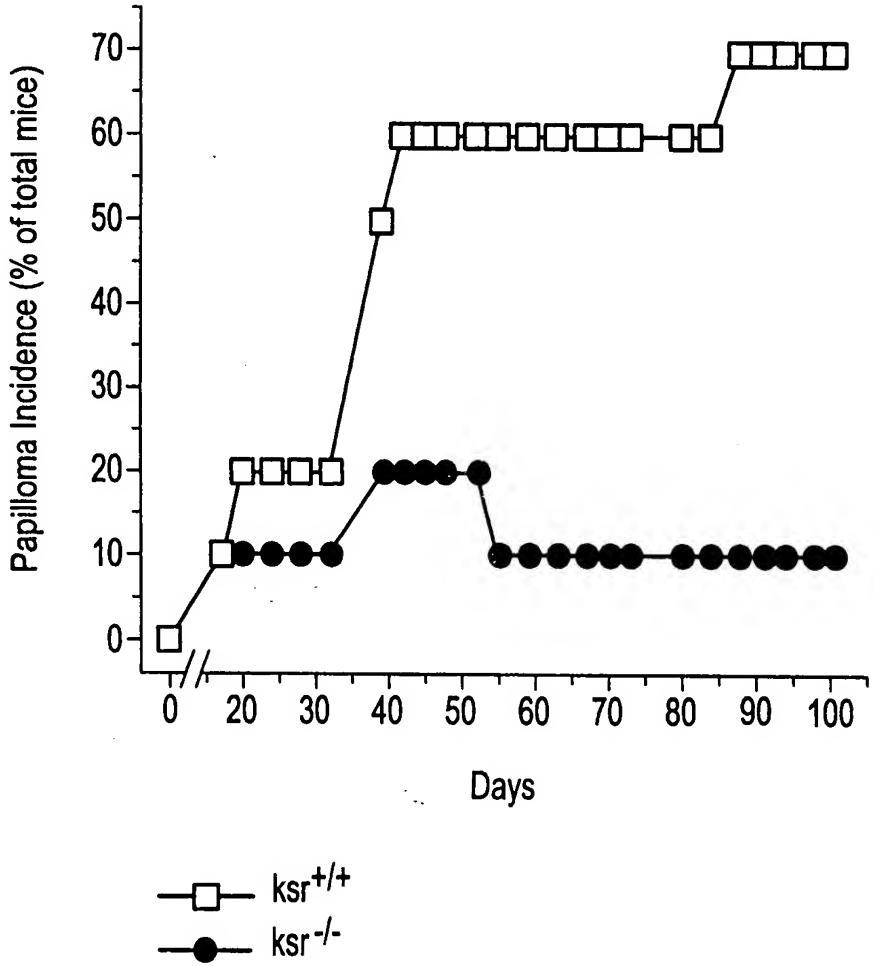

Papilloma Incidence (% of total mice)
70
60
50
40
30
20
10
0
0
20
30
40
50
60
70
80
90
100
Days
ksr+/+
ksr-/-

FIG. 5A

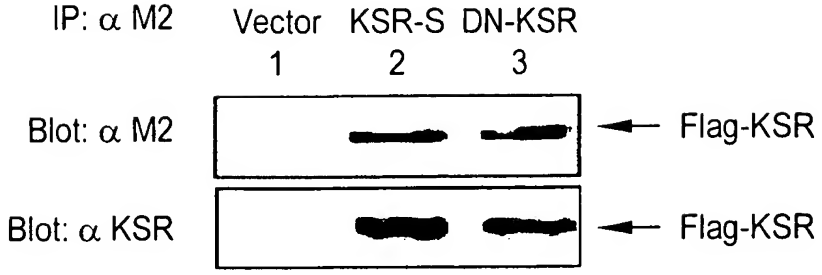


FIG. 5B

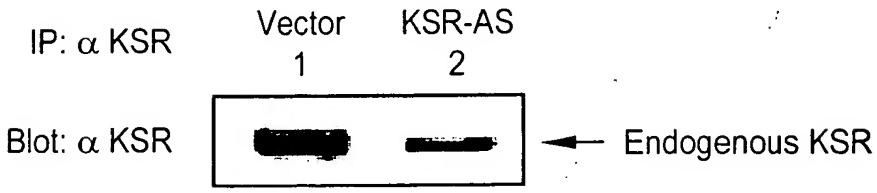


FIG. 5C

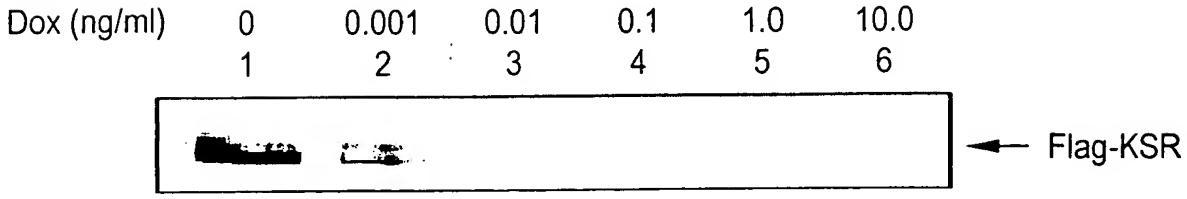


FIG. 5D

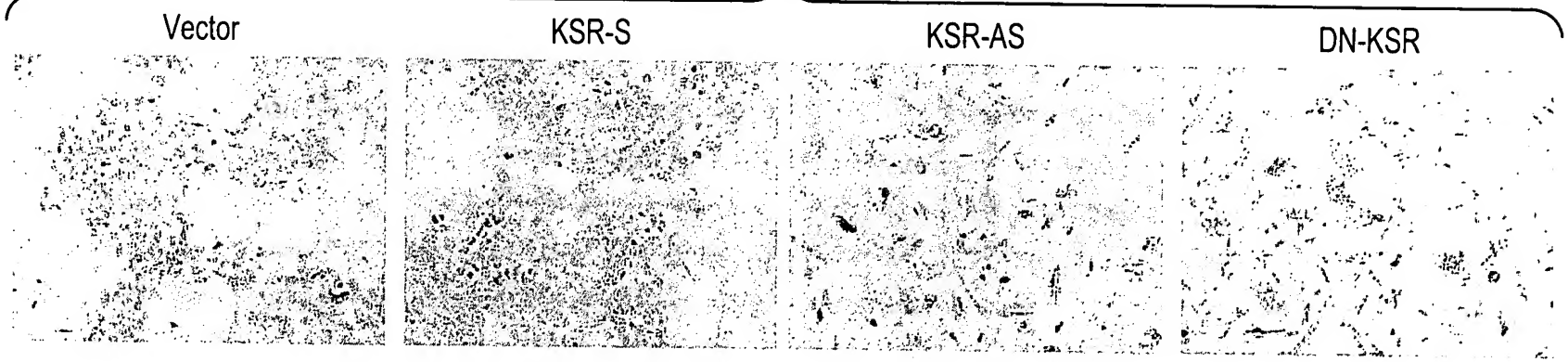


FIG. 5E

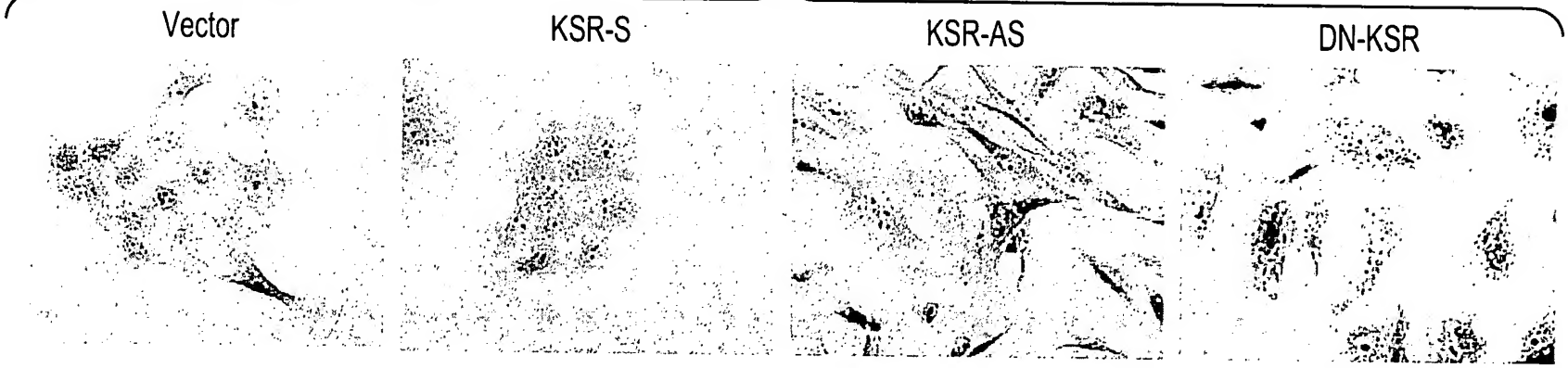


FIG. 6A

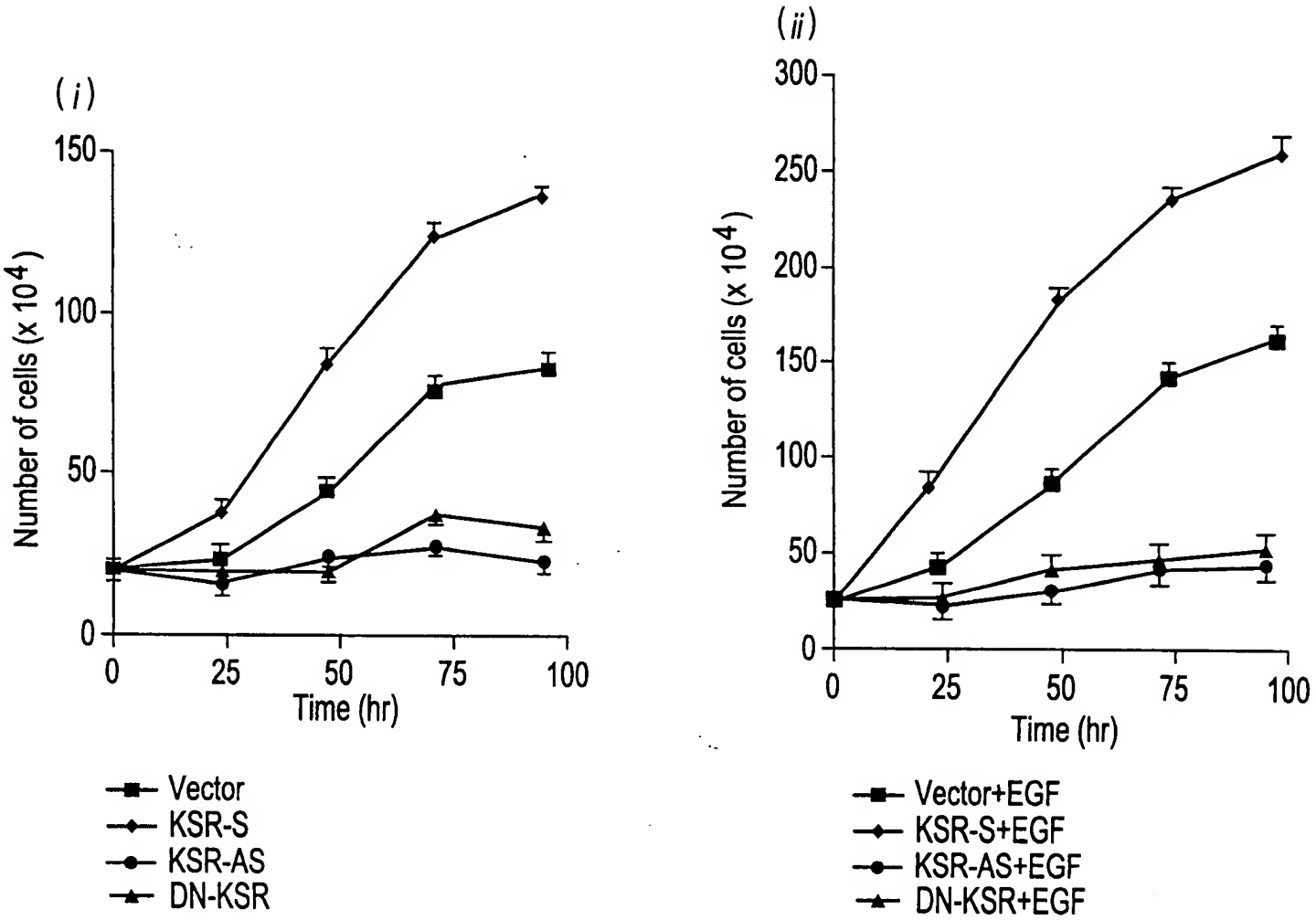

(i)
Number of cells (x 10^4)
150
100
50
0
0
25
50
75
100
Time (hr)
Vector
KSR-S
KSR-AS
DN-KSR
(ii)
Number of cells (x 10^4)
300
250
200
150
100
50
0
0
25
50
75
100
Time (hr)
Vector+EGF
KSR-S+EGF
KSR-AS+EGF
DN-KSR+EGF

FIG. 6B

	% G1	% S	% G2
Vector	40.1	45.1	14.8
KSR-S	25.2	60.8	14.0
KSR-AS	16.4	23.2	60.4
DN-KSR	24.2	24.8	51.0

FIG. 6C

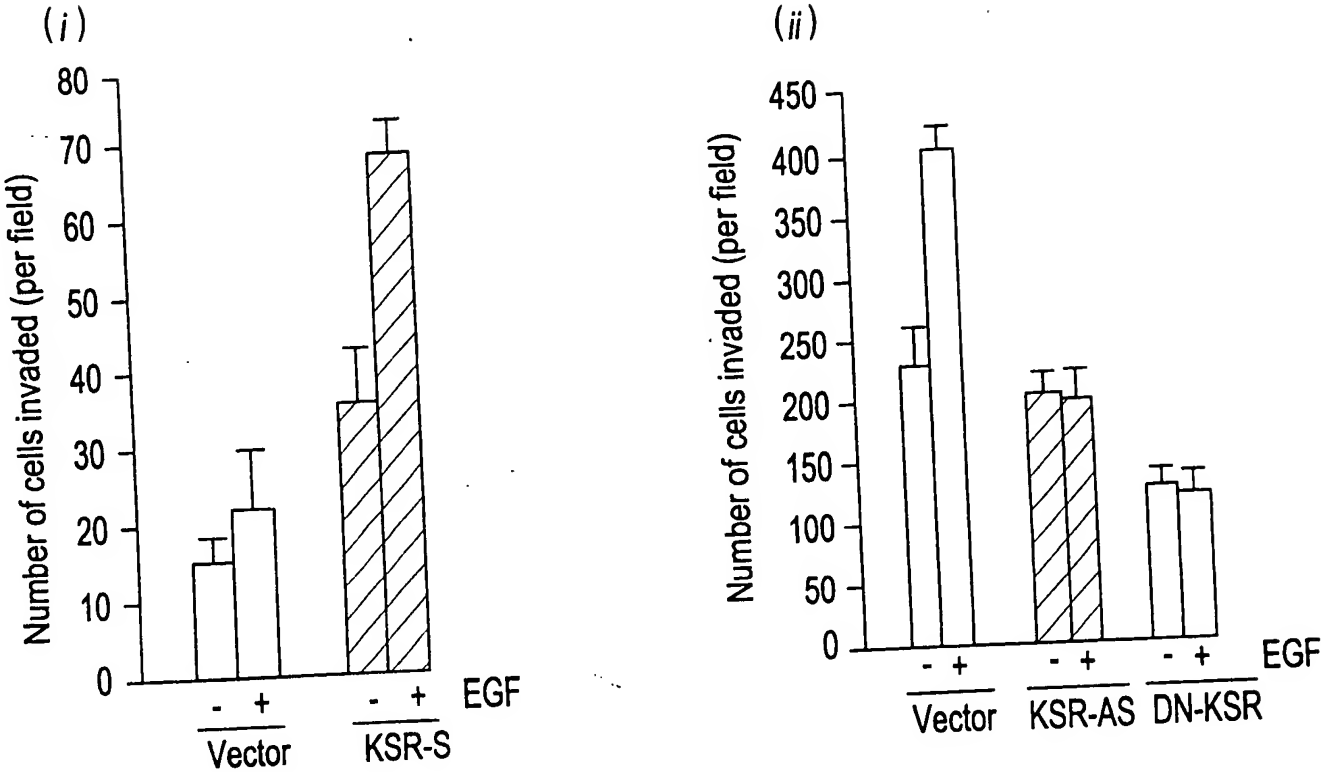

(i)
Number of cells invaded (per field)
80
70
60
50
40
30
20
10
0
- + - +
EGF
Vector
KSR-S
(ii)
Number of cells invaded (per field)
450
400
350
300
250
200
150
100
50
0
- + - + - +
EGF
Vector
KSR-AS
DN-KSR

FIG. 6D

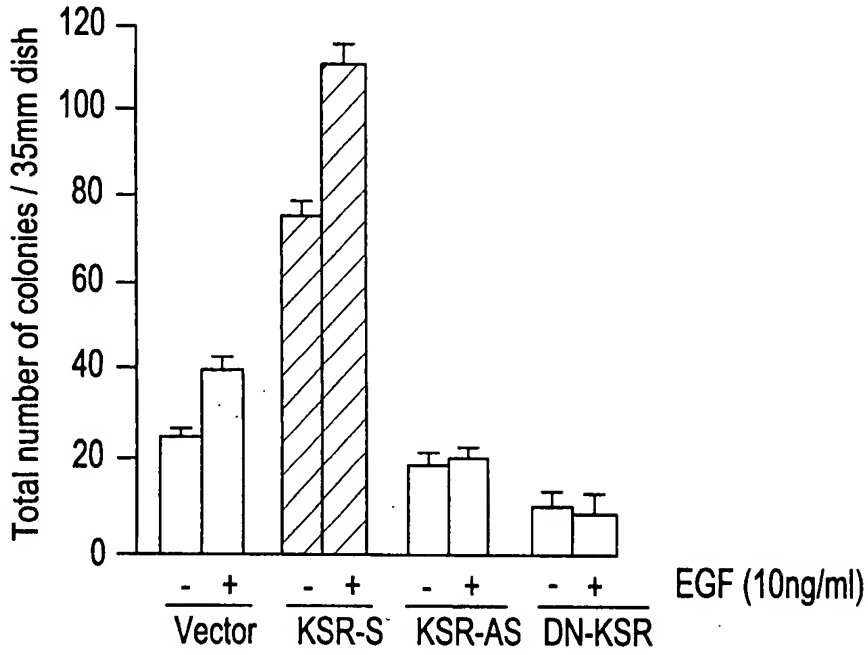

Total number of colonies / 35mm dish
120
100
80
60
40
20
0
- +
- +
- +
- +
EGF (10ng/ml)
Vector
KSR-S
KSR-AS
DN-KSR

FIG. 7A

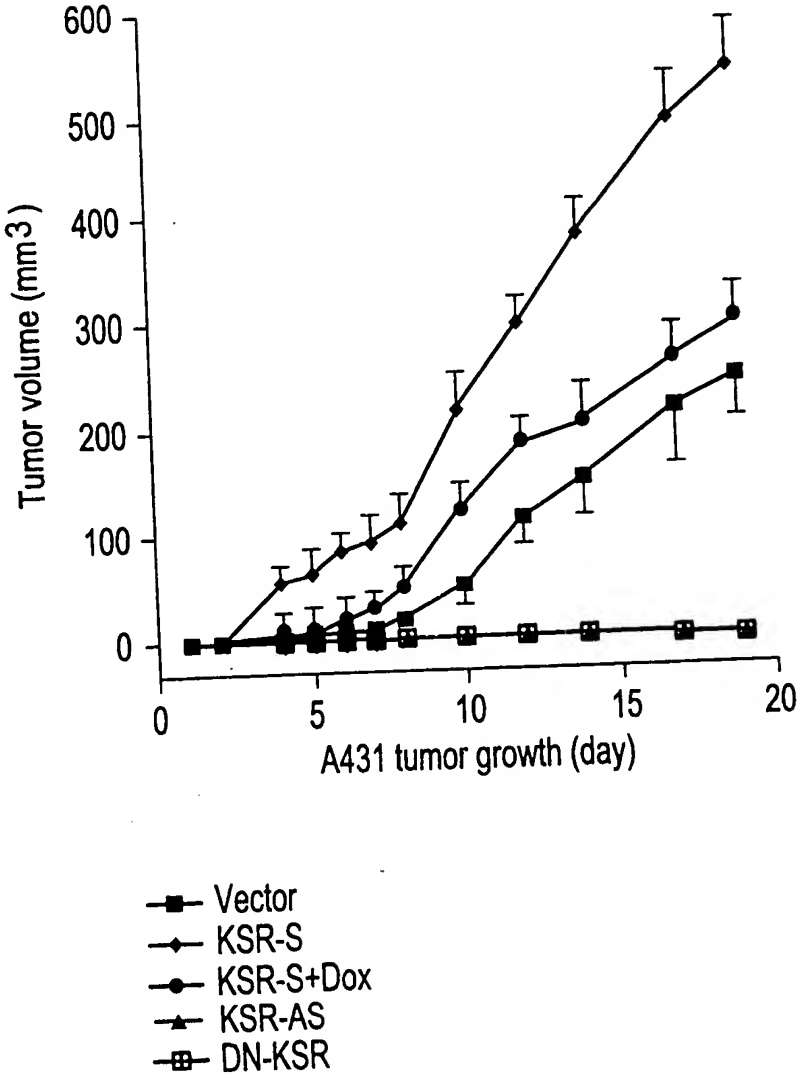

600
500
400
300
200
100
0
Tumor volume (mm3)
0
5
10
15
20
A431 tumor growth (day)
Vector
KSR-S
KSR-S+Dox
KSR-AS
DN-KSR

FIG. 7B

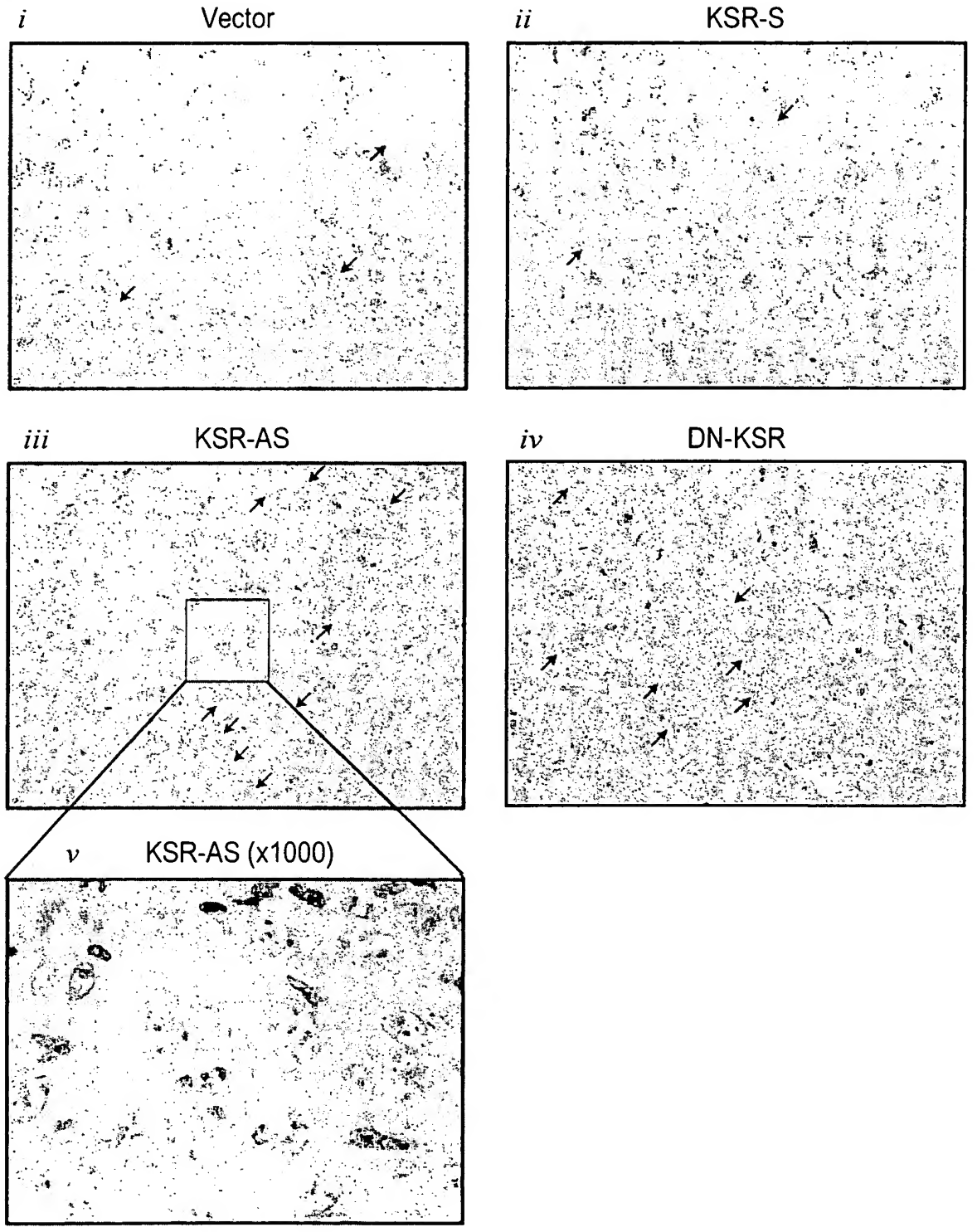


FIG. 8A

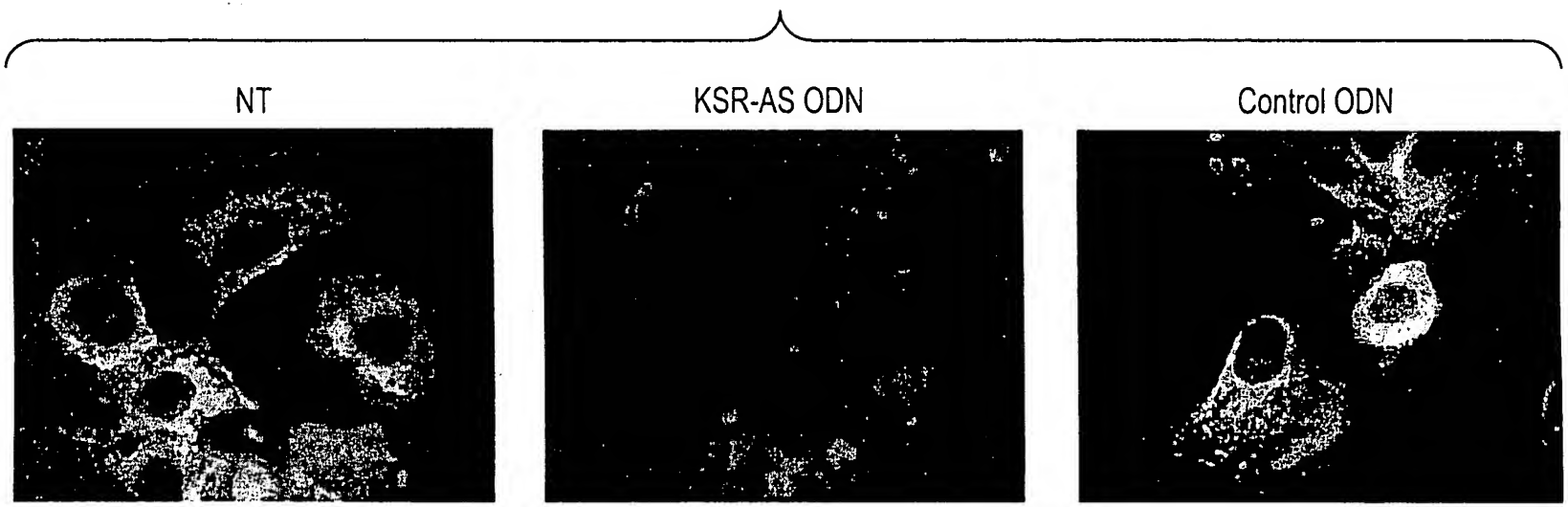


FIG. 8B

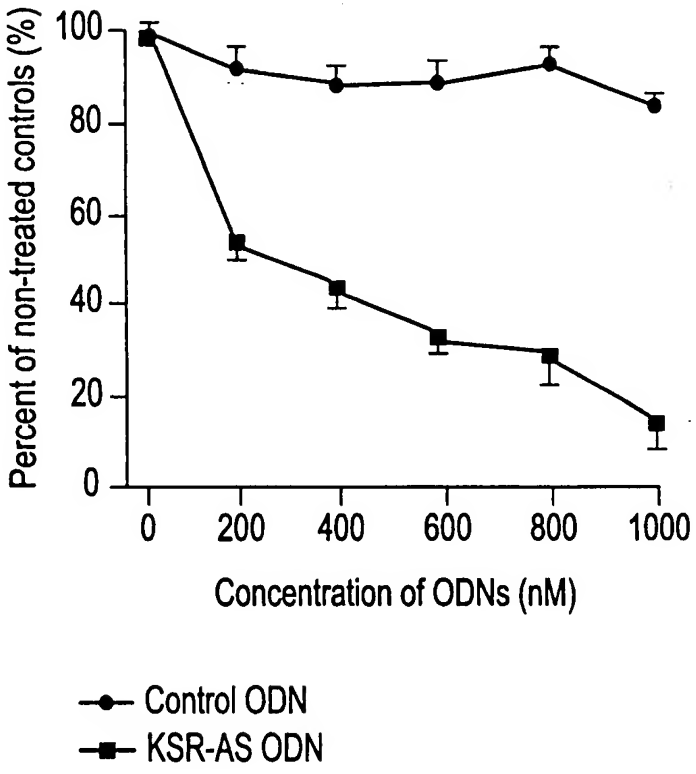

Percent of non-treated controls (%)
100
80
60
40
20
0
0
200
400
600
800
1000
Concentration of ODNs (nM)
Control ODN
KSR-AS ODN

FIG. 8C

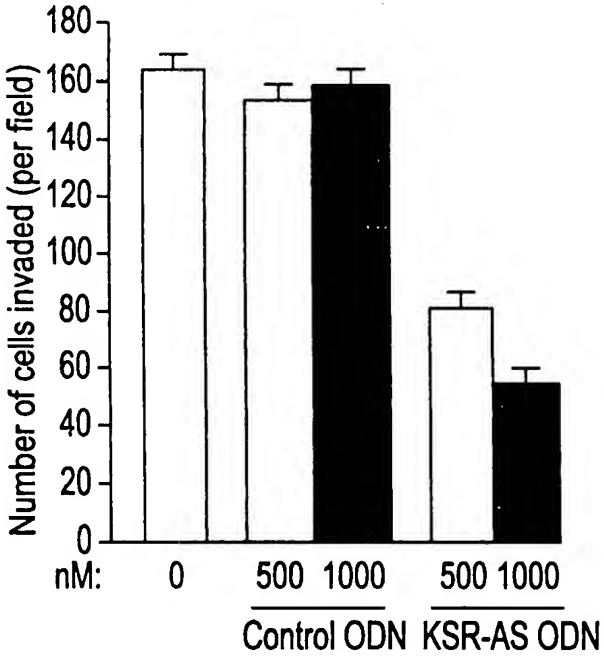

Number of cells invaded (per field)
180
160
140
120
100
80
60
40
20
0
nM:
0
500
1000
500
1000
Control ODN
KSR-AS ODN

FIG. 8D

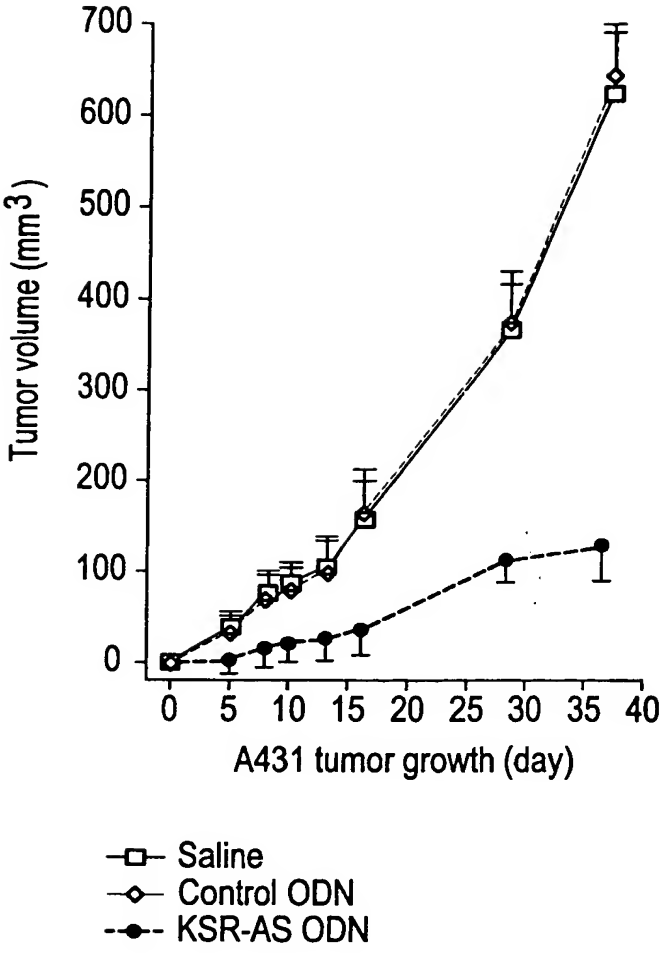

700
600
500
400
300
200
100
0
Tumor volume (mm3)
0 5 10 15 20 25 30 35 40
A431 tumor growth (day)
Saline
Control ODN
KSR-AS ODN

FIG. 9A

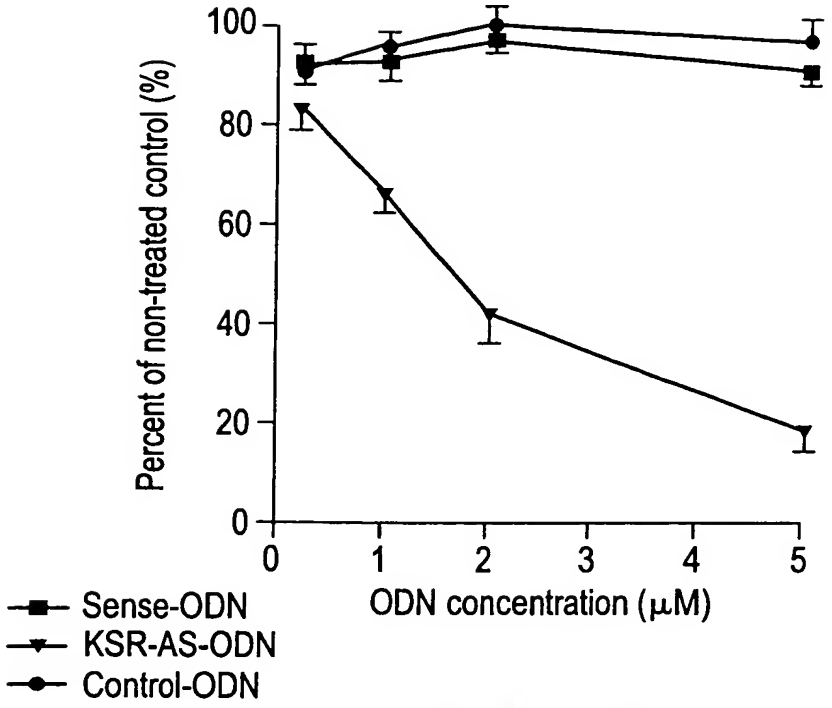

Percent of non-treated control (%)
100
80
60
40
20
0
0
1
2
3
4
5
ODN concentration (μM)
Sense-ODN
KSR-AS-ODN
Control-ODN

FIG. 9B

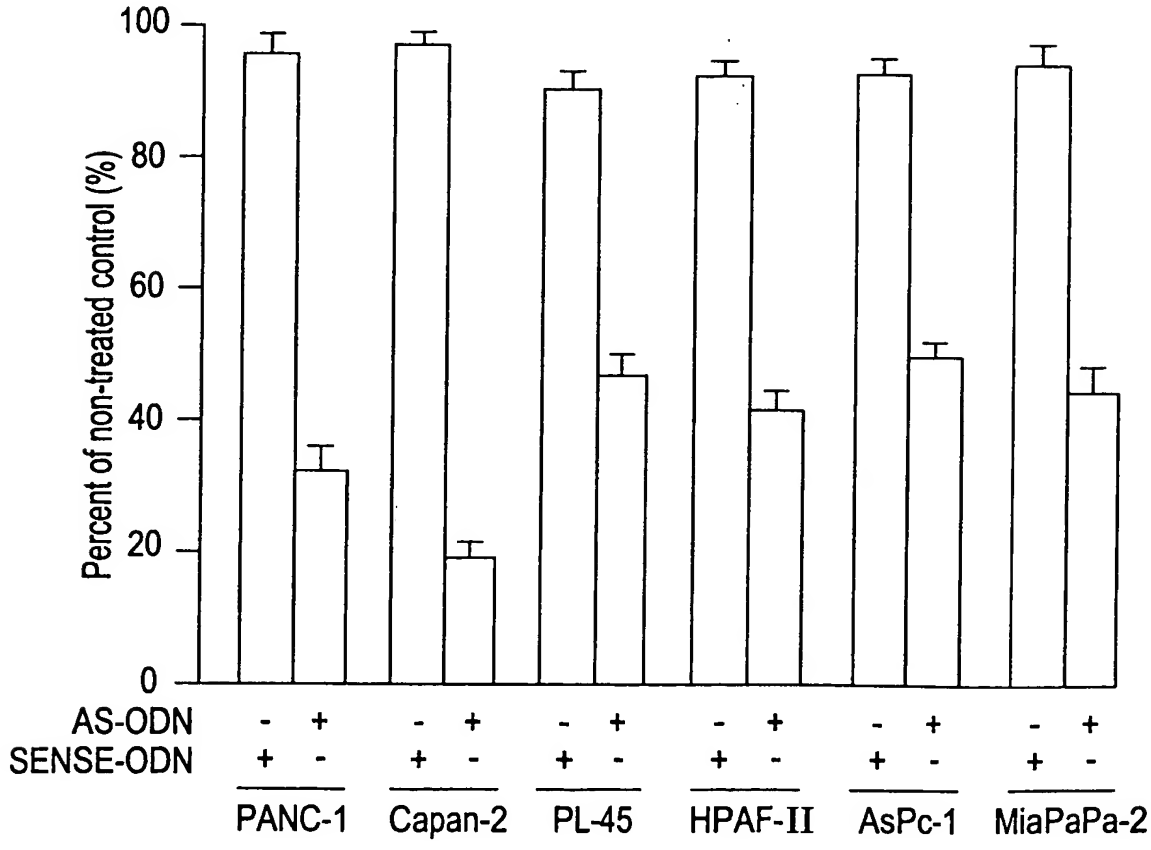

Percent of non-treated control (%)
100
80
60
40
20
0
AS-ODN
SENSE-ODN
PANC-1
Capan-2
PL-45
HPAF-II
AsPc-1
MiaPaPa-2

FIG. 9C

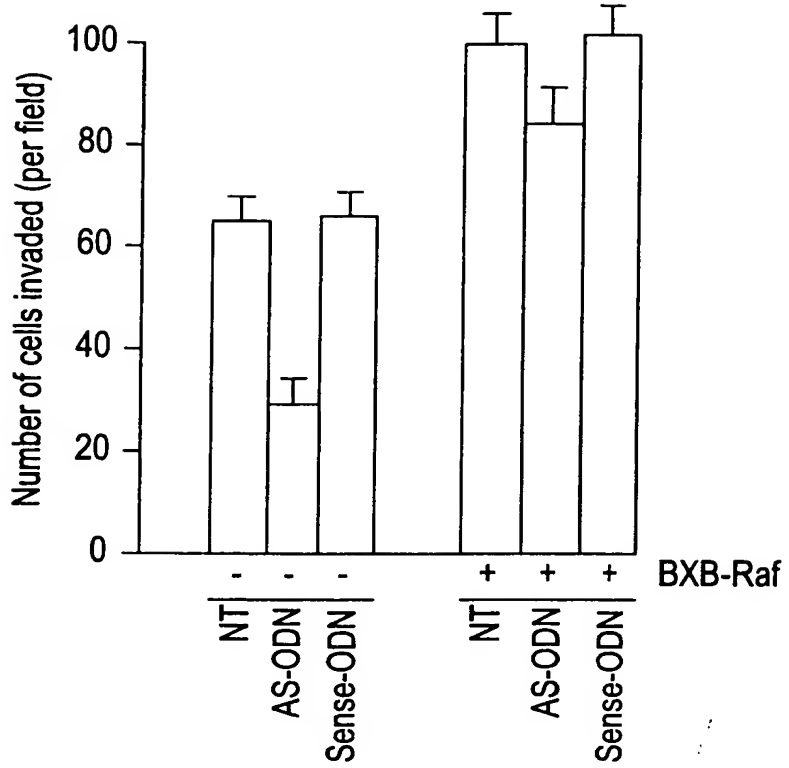

Number of cells invaded (per field)
100
80
60
40
20
0
- - - + + +
BXB-Raf
NT
AS-ODN
Sense-ODN
NT
AS-ODN
Sense-ODN

FIG. 9D

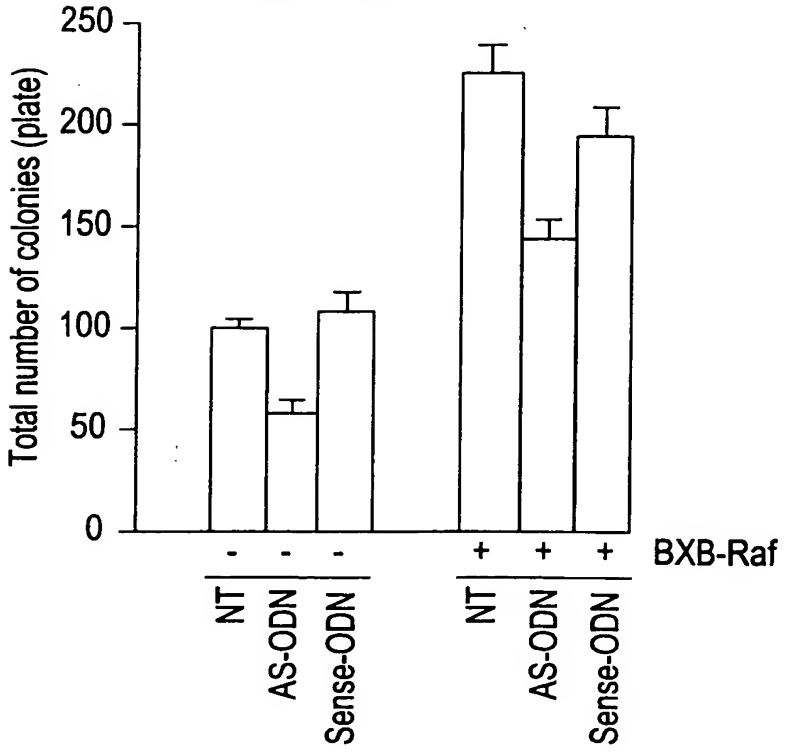

Total number of colonies (plate)
250
200
150
100
50
0
- - - + + +
BXB-Raf
NT
AS-ODN
Sense-ODN
NT
AS-ODN
Sense-ODN

FIG. 9E

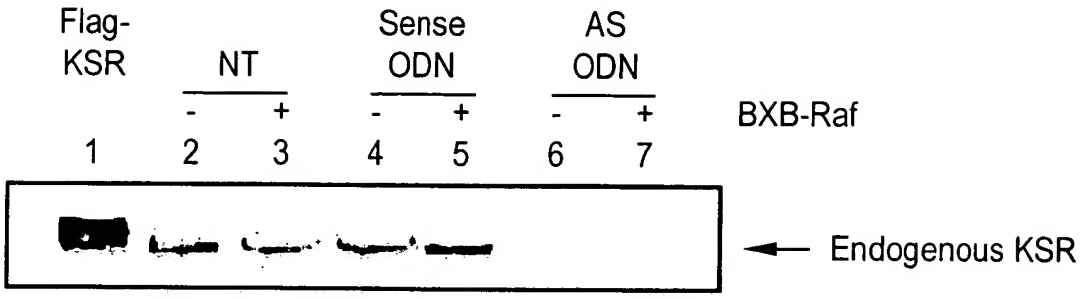

Flag-KSR
NT
Sense ODN
AS ODN
- + - + - +
1 2 3 4 5 6 7
BXB-Raf
Endogenous KSR

FIG. 9F

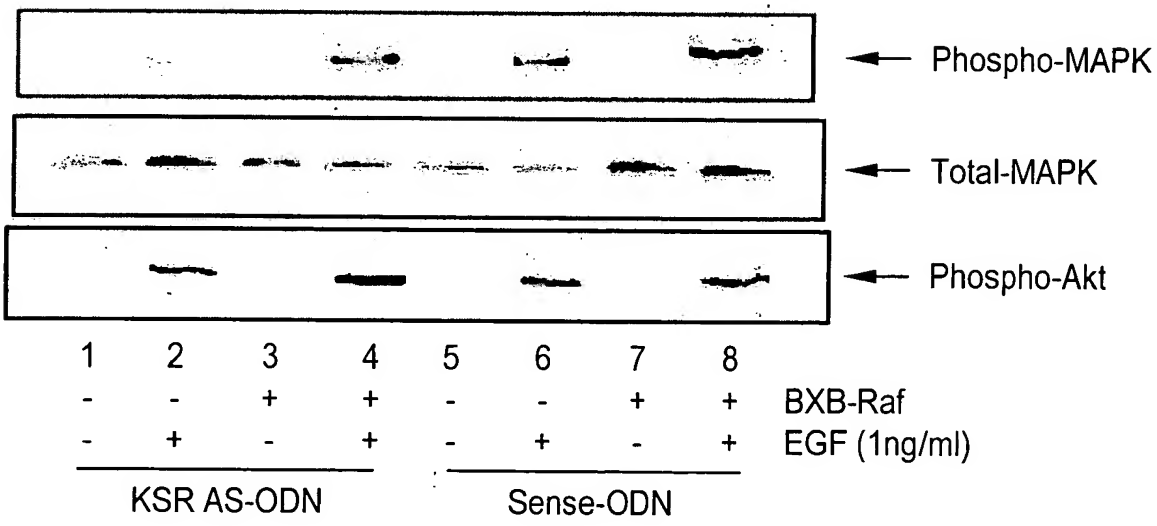

Phospho-MAPK
Total-MAPK
Phospho-Akt
1 2 3 4 5 6 7 8
- - + + - - + + BXB-Raf
- + - + - + - + EGF (1ng/ml)
KSR AS-ODN
Sense-ODN

FIG. 10A

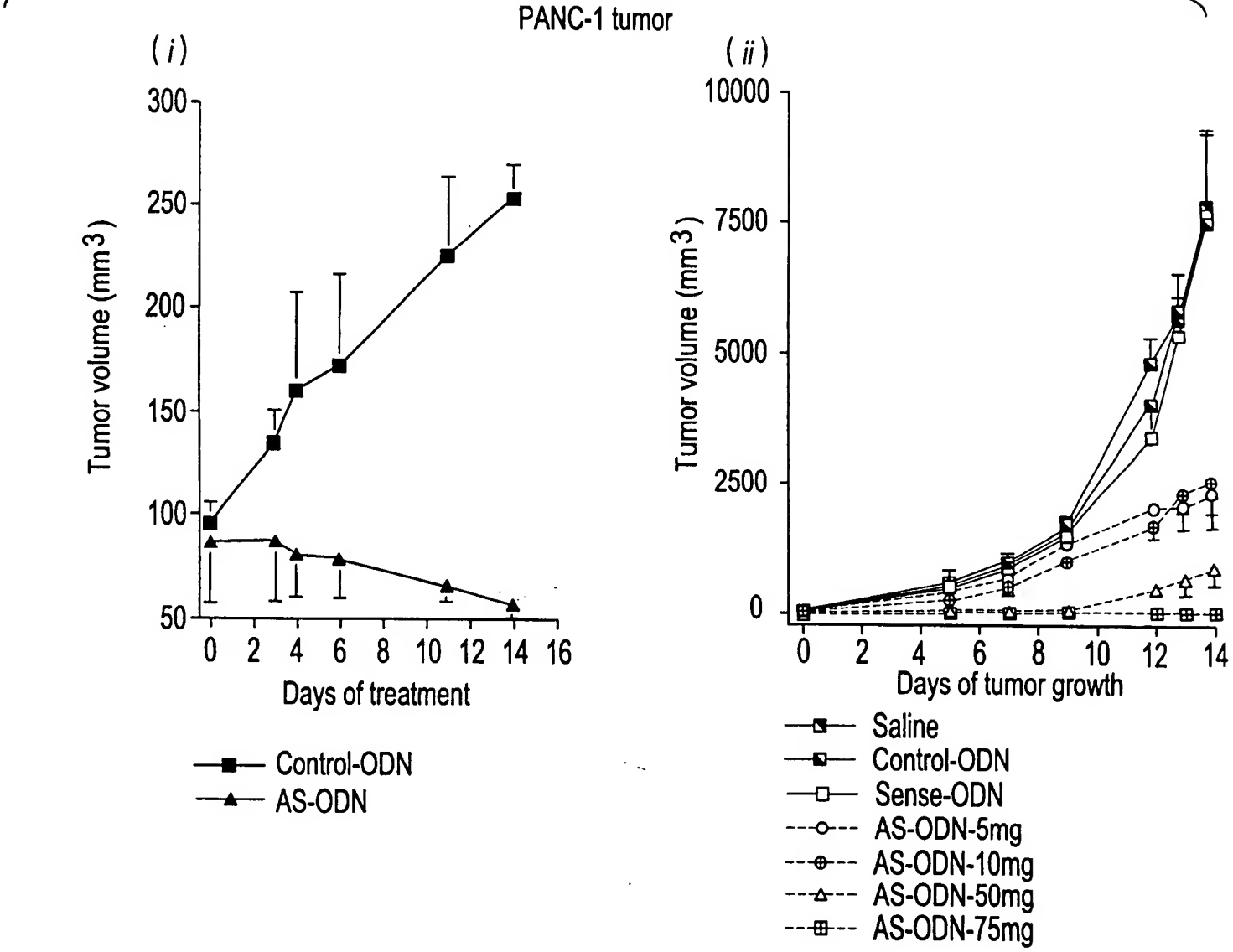

PANC-1 tumor
(i)
Tumor volume (mm3)
300
250
200
150
100
50
0 2 4 6 8 10 12 14 16
Days of treatment
Control-ODN
AS-ODN
(ii)
Tumor volume (mm3)
10000
7500
5000
2500
0
0 2 4 6 8 10 12 14
Days of tumor growth
Saline
Control-ODN
Sense-ODN
AS-ODN-5mg
AS-ODN-10mg
AS-ODN-50mg
AS-ODN-75mg

FIG. 10B

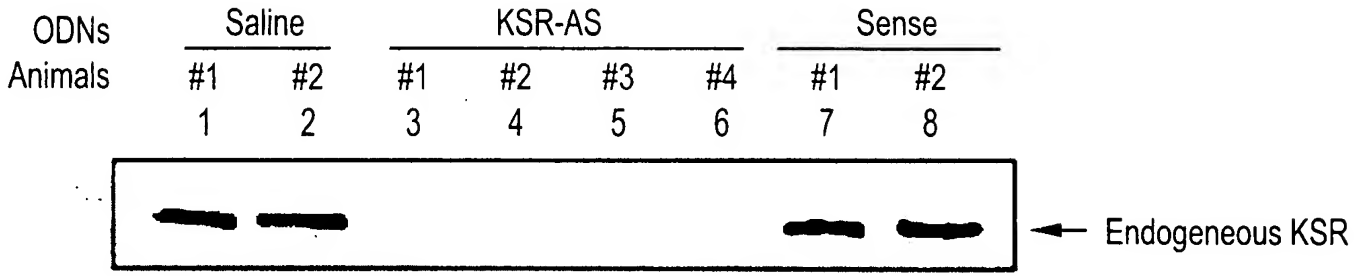


FIG. 10C

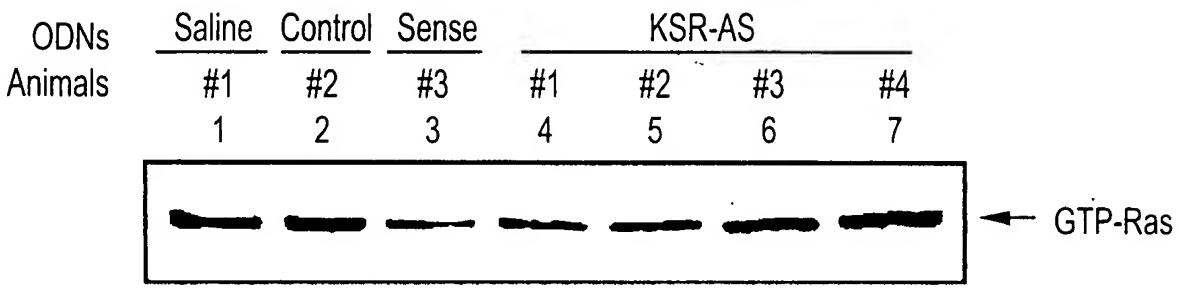
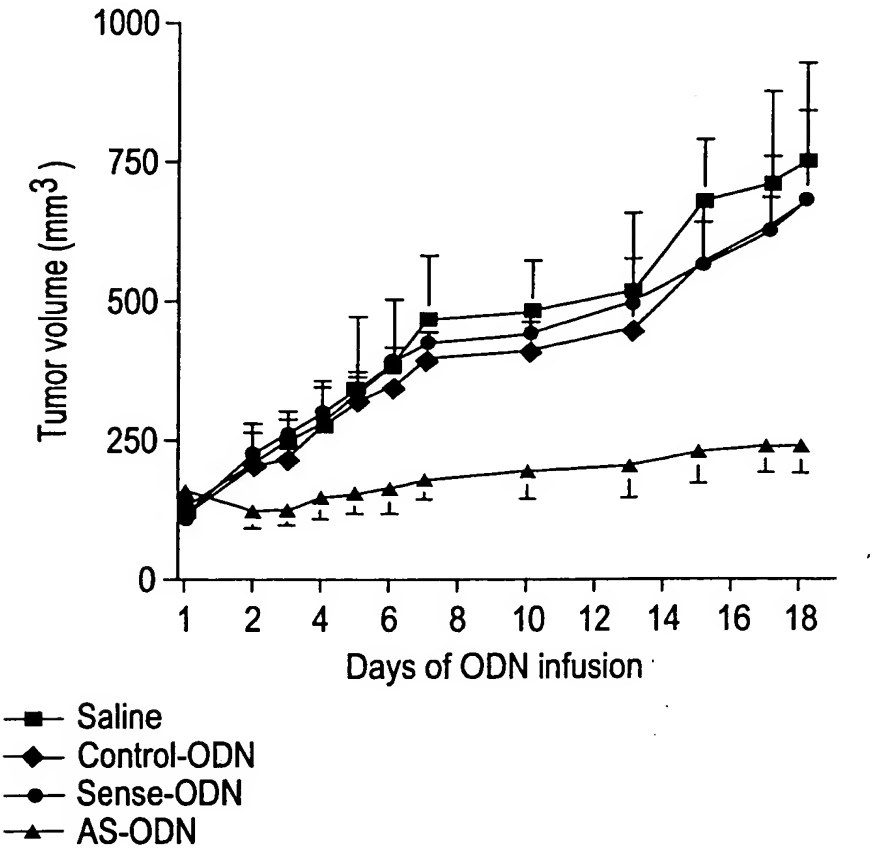


FIG. 10D

A549 tumor

(*i*)



(*ii*)

Number of lung metastases foci
(whole lung surface)

Dose of infusion (mg/ kg /Day)	Sense-ODNs	AS-ODN	% inhibition
10	7.4 ± 1.4	2.5 ± 0.6	65
25	10.2 ± 1.8	1.4 ± 0.5	86

**** FIG.11-1

```
Human              MGEK-EGGGGGDAAAAEGGAGAAASRALQQCGQLQ     34
Mouse MDRAALRAAA     K       --           V

                          CA1
Human KLIDISIGSLRGLRTKCAVSNDLTQQEIRTLEAKLVRYICKQRQC     79
Mouse                     S                    K     Q S

Human KLSVAPGERTPELNSYPRFSDWLYTFNVRPEVVQEIPRDLTLDAL    124
Mouse     I SD  A               I            QE

Human LEMNEAKVKETLRRCGASGDECGRLQYALTCLRKVTGLGGEHKED    169
Mouse    D   A  M   W   TE  S   Q                 M

Human SSWSSLDARRESGSGPSTDTLSAASLPWPPGSSQLGRAGNSAQGP    214
Mouse  G   I   DS -L  PM M  S-----------     A T

                                                  →
Human RSISVSALPASDSPTPSFSEGLSDTCIPLHASGRLTPRALHSFIT    259
Mouse               V GL     S      I

                          CA2
Human PPTTPQLRRHTKLKPPRTPPPPSRKVFQLLPSFPTLTRSKSHESQ    304
MouseA

Human LGNRIDDVSSMRFDLSHGSPQMVRRDIGLSVTHRFSTKSWLSQVC    349
Mouse         TP K E P     L

                          CA3
Human HVCQKSMIFGVKCKHCRLKCHNKCTKEAPACRISFLPLTRLRRTE    394
Mouse N                                  I    A

Human SVPSDINNPVDRAAEPHFGTLPKALTKKEHPPAMNHLDSSSNPSS    439
Mouse                                    -

                          CA4
Human TTSSTPSSPAPFPTSSNPSSATTPPNPSPGQRDSRFNFPAAYFIH    484
Mouse              L                        S -------

Human HRQQFIFPDISAFAHAAPLPEAADGTRLDDQPKADVLEAHEAEAE    529
Mouse --------     CSC    SST  S        I   GV

Human EPEAGKSEAEDDED-EVDDLPSSRRPWRGPISRKASQTSVYLQEW    573
Mouse               ED
```

FIG. 11-2

```
                          I              II
Human DDIPFEQVELGEPIGQGRWGRVHRGRWHGEVAIRLLEMDGHNQDH   618
Mouse

         III              IV                        V
Human LKLFKKEVMNYRQTRHENVVLFMGACMNPPHLAIITSFCKGRTLH   663
Mouse

                                    VIa          VIb
Human SFVRDPKTSLDINKTRQIAQEIIKGMGYLHAKGIVHKDLKSKNVF   708
Mouse

               VII                              VIII
Human YDNGKVVITDFGLFGISGVVREERRENQLKLSHDWLCYLAPEIVR   753
Mouse

                              IX
Human EMTPGKDEDQLPFSKAADVYAFGTVWYELQARDWPLKNQAAEASI   798
Mouse   I  R                                F H P   L
       X                             XI
Human WQIGSGEGMKRVLTSVSLGKEVSEILSACWAFDLQERPSFSLLMD   843
Mouse         VR   A        G


Human MLEKLPKLNRRLSHPGHFWKSAEL                         867
Mouse    R                   DINSSKVMPRFERFGLGTLESGN

Mouse PKM
```

FIG. 12A-1

```
1     GAATTCCCTC GGGGCTTTCC TGCCGAGGCG CCCGTGTCCC CGGGCTCCTC GCCTCGGCCC
61    CCAGCGGCCC CGATGCCGAG GCATGGATAG AGCGGCGTTG CGCGCGGCAG CGATGGGCGA
121   GAAAAAGGAG GGCGGCGGCG GGGGCGCCGC GGCGGACGGG GGCGCAGGGG CCGCCGTCAG
181   CCGGGCGCTG CAGCAGTGCG GCCAGCTGCA GAAGCTCATC GATATCTCCA TCGGCAGTCT
241   GCGCGGGCTG CGCACCAAGT GCTCAGTGTC TAACGACCTC ACACAGCAGG AGATCCGGAC
301   CCTAGAGGCA AAGCTGGTGA AATACATTTG CAAGCAGCAG CAGAGCAAGC TTAGTGTGAC
361   CCCAAGCGAC AGGACCGCCG AGCTCAACAG CTACCCACGC TTCAGTGACT GGCTGTACAT
421   CTTCAACGTG AGGCCTGAGG TGGTGCAGGA GATCCCCCAA GAGCTCACAC TGGATGCTCT
481   GCTGGAGATG GACGAGGCCA AAGCCAAGGA GATGCTGCGG CGCTGGGGGG CCAGCACGGA
541   GGAGTGCAGC CGCCTACAGC AAGCCCTTAC CTGCCTTCGG AAGGTGACTG GCCTGGGAGG
601   GGAGCACAAA ATGGACTCAG GTTGGAGTTC AACAGATGCT CGAGACAGTA GCTTGGGGCC
661   TCCCATGGAC ATGCTTTCCT CGCTGGGCAG AGCGGGTGCC AGCACTCAGG GACCCCGTTC
721   CATCTCCGTG TCCGCCCTGC CTGCCTCAGA CTCTCCGGTC CCCGGCCTCA GTGAGGGCCT
781   CTCGGACTCC TGTATCCCCT TGCACACCAG CGGCCGGCTG ACCCCCCGGG CCCTGCACAG
841   CTTCATCACG CCCCCTACCA CACCCCAGCT ACGACGGCAC GCCAAGCTGA AGCCACCAAG
901   GACACCCCCA CCGCCAAGCC GCAAGGTCTT CCAGCTGCTC CCCAGCTTCC CCACACTCAC
961   ACGGAGCAAG TCCCACGAGT CCCAGCTGGG AAACCGAATC GACGACGTCA CCCCGATGAA
1021  GTTTGAACTC CCTCATGGAT CCCCACAGCT GGTACGAAGG GATATCGGGC TCTCGGTGAC
1081  GCACAGGTTC TCCACAAAGT CATGGTTGTC ACAGGTGTGC AACGTGTGCC AGAAGAGCAT
1141  GATTTTTGGC GTGAAGTGCA AACACTGCAG GTTAAAATGC CATAACAAGT GCACAAAGGA
1201  AGCTCCCGCC TGCAGGATCA CCTTCCTCCC ACTGGCCAGG CTTCGGAGGA CAGAGTCTGT
1261  CCCGTCAGAT ATCAACAACC CAGTGGACAG AGCAGCAGAG CCCCATTTTG GAACCCTTCC
1321  CAAGGCCCTG ACAAAGAAGG AGCACCCTCC AGCCATGAAC CTGGACTCCA GCAGCAACCC
1381  ATCCTCCACC ACGTCCTCCA CACCCTCATC GCCGGCACCT TTCCTGACCT CATCTAATCC
1441  CTCCAGTGCC ACCACGCCTC CCAACCCGTC ACCTGGCCAG CGGGACAGCA GGTTCAGCTT
1501  CCCAGACATT TCAGCCTGTT CTCAGGCAGC CCCGCTGTCC AGCACAGCCG ACAGTACACG
1561  GCTCGACGAC CAGCCCAAAA CAGATGTGCT AGGTGTTCAC GAAGCAGAGG CTGAGGAGCC
1621  TGAGGCTGGC AAGTCAGAGG CAGAGGATGA CGAGGAGGAT GAGGTGGACG ACCTCCCCAG
1681  CTCCCGCCGG CCCTGGAGGG GCCCCATCTC TCGAAAGGCC AGCCAGACCA GCGTTTACCT
1741  GCAAGAGTGG GACATCCCCT TTGAACAGGT GGAACTGGGC GAGCCCATTG GACAGGGTCG
1801  CTGGGGCCGG GTGCACCGAG GCCGTTGGCA TGGCGAGGTG GCCATTCGGC TGCTGGAGAT
1861  GGACGGCCAC AATCAGGACC ACCTGAAGCT GTTCAAGAAA GAGGTGATGA ACTACCGGCA
1921  GACGCGGCAT GAGAACGTGG TGCTCTTCAT GGGGGCCTGC ATGAACCCAC CTCACCTGGC
1981  CATTATCACC AGCTTCTGCA AGGGGCGGAC ATTGCATTCA TTCGTGAGGG ACCCCAAGAC
2041  GTCTCTGGAC ATCAATAAGA CTAGGCAGAT CGCCCAGGAG ATCATCAAGG GCATGGGTTA
2101  TCTTCATGCA AAAGGCATCG TGCACAAGGA CCTCAAGTCC AAGAATGTCT TCTATGACAA
2161  CGGCAAAGTG GTCATCACAG ACTTCGGGCT GTTTGGGATC TCGGGTGTGG TCCGAGAGGA
2221  ACGGCGCGAG AACCAACTGA AACTGTCACA TGACTGGCTG TGCTACCTGG CCCCCGAGAT
2281  CGTACGAGAA ATGATCCCGG GGCGGGACGA GGACCAGCTG CCCTTCTCCA AAGCAGCCGA
2341  TGTCTATGCA TTCGGGACTG TGTGGTATGA ACTACAGGCA AGAGACTGGC CCTTTAAGCA
2401  CCAGCCTGCT GAGGCCTTGA TCTGGCAGAT TGGAAGTGGG GAAGGAGTAC GGCGCGTCCT
2461  GGCATCCGTC AGCCTGGGGA AGGAAGTCGG CGAGATCCTG TCTGCCTGCT GGGCTTTCGA
2521  TCTGCAGGAG AGACCCAGCT TCAGCCTGCT GATGGACATG CTGGAGAGGC TGCCCAAGCT
2581  GAACCGGCGG CTCTCCCACC CTGGGCACTT TTGGAAGTCG GCTGACATTA ACAGCAGCAA
2641  AGTCATGCCC CGCTTTGAAA GGTTTGGCCT GGGGACCCTG GAGTCCGGTA ATCCAAAGAT
```

FIG. 12A-2

```
2701 GTAGCCAGCC CTGCACGTTC ATGCAGAGAG TGTCTTCCTT TCGAAAACAT GATCACGAAA
2761 CATGCAGACC ACCACCTCAA GGAATCAGAA GCATTGCATC CCAAGCTGCG GACTGGGAGC
2821 GTGTCTCCTC CCTAAAGGAC GTGCGTGCGT GCGTGCGTGC GTGCGTGCGT GCGTGCGTCA
2881 CCAAGGTGTG TGGAGCTCAG GATCGCAGCC ATACACGCAA CTCCAGATGA TACCACTACC
2941 GCCAGTGTTT ACACAGAGGT TTCTGCCTGG CAAGCTTGGT ATTTTACAGT AGGTGAAGAT
3001 CATTCTGCAG AAGGGTGCTG GCACAGTGGA GCAGCACGGA TGTCCCCAGC CCCCGTTCTG
3061 GAAGACCCTA CAGCTGTGAG AGGCCCAGGG TTGAGCCAGA TGAAAGAAAA GCTGCGTGGG
3121 TGTGGGCTGT ACCCGGAAAA GGGCAGGTGG CAGGAGGTTT GCCTTGGCCT GTGCTTGGGC
3181 CGAGAACCAC ACTAAGGAGC AGCAGCCTGA GTTAGGAATC TATCTGGATT ACGGGGATCA
3241 GAGTTCCTGG AGAGTGGACT CAGTTTCTGC TCTGATCCAG GCCTGTTGTG CTTTTTTTTT
3301 TTCCCCCTTA AAAAAAAAAA AGTACAGACA GAATCTCAGC GGCTTCTAGA CTGATCTGAT
3361 GGATCTTAGC CCGGCTTCTA CTGCGGGGGG GAGGGGGGGA GGGATAGCCA CATATCTGTG
3421 GAGACACCCA CTTCTTTATC TGAGGCCTCC AGGTAGGCAC AAAGGCTGTG GAACTCAGCC
3481 TCTATCATCA GACACCCCCC CCCAATGCCT CATTGACCCC CTTCCCCCAG AGCCAAGGGC
3541 TAGCCCATCG GGTGTGTGTA CAGTAAGTTC TTGGTGAAGG AGAACAGGGA CGTTGGCAGA
3601 AGCAGTTTGC AGTGGCCCTA GCATCTTAAA ACCCATTGTC TGTCACACCA GAAGGTTCTA
3661 GACCTACCAC CACTTCCCTT CCCCATCTCA TGGAAACCTT TTAGCCCATT CTGACCCCTG
3721 TGTGTGCTCT GAGCTCAGAT CGGGTTATGA GACCGCCCAG GCACATCAGT CAGGGAGGCT
3781 CTGATGTGAG CCGCAGACCT CTGTGTTCAT TCCTATGAGC TGGAGGGGCT GGACTGGGTG
3841 GGGTCAGATG TGCTTGGCAG GAACTGTCAG CTGCTGAGCA GGGTGGTCCC TGAGCGGAGG
3901 ATAAGCAGCA TCAGACTCCA CAACCAGAGG AAGAAAGAAA TGGGGATGGA GCGGAGACCC
3961 ACGGGCTGAG TCCCGCTGTG GAGTGGCCTT GCAGCTCCCT CTCAGTTAAA ACTCCCAGTA
4021 AAGCCACAGT TCTCCGAGCA CCCAAGTCTG CTCCAGCCGT CTCTTAAAAC AGGCCACTCT
4081 CTGAGAAGGA ATTC
```

FIG. 12B-1

```
1     GCGAAGCTGG TCCGTTACAT TTGTAAGCAG AGGCAGTGCA AGCTGAGCGT GGCTCCCGGT
61    GAGAGGACCC CAGAGCTCAA CAGCTACCCC CGCTTCAGCG ACTGGCTGTA CACTTTCAAC
121   GTGAGGCCGG AGGTGGTGCA GGAGATCCCC CGAGACCTCA CGCTGGATGC CCTGCTGGAG
181   ATGAATGAGG CCAAGGTGAA GGAGACGCTG CGGCGCTGTG GGGCCAGCGG GGATGAGTGT
241   GGCCGTCTGC AGTATGCCCT CACCTGCCTG CGGAAGGTGA CAGGCCTGGC TTCATCACCC
301   CGCCCACCAC ACCCCAGCTG CGACGGCACA CCAAGCTGAA GCCACCACGG ACGCCCCCCC
361   CACCCAGCCG CAAGGTCTTC CAGCTGCTGC CCAGCTTCCC CACACTCACC CGGAGCAAGT
421   CCCATGAGTC TCAGCTGGGG AACCGCATTG ATGACGTCTC CTCGATGAGG TGAGTTGGGA
481   GCACGTTCCT GCACGTGGCT ATGCTGTGGG GCCTCTCTCA TGAGTCAGAG CGGAGGGAGA
541   CAGCTGTGCC TCTGGAGTCT GCTTTTAATT GTCTGGAAAT GCAGAGATGT CTGGTTTTTG
601   CCTGAGCAAA ATAGGAGTTT ATTTTTGTAC TATCCCGAGC TGGCTAAGGA GAGTCACGTA
661   GCTGTGGGCG GGGTCTTGGG GATGAGGAGG GGTACAGCAG GCAGGGACTA TGCTGAAGTG
721   GAGCTGGCTG TAGGAACCCC AGGGAGGCAC AGGGGGAGCA TGAAGAGGAG CTACACTTCC
781   CTCCCTTAGT GCCCGGGCAG AAACTCCCAG GGCCCTTCAC AGAACCTTGG AGGAACATTC
841   AACACCCCCA TCTCTAGGAC AGCCCCAGCC TTGTCATCCT CCAATTGCTG TGGTAACACG
901   GGGACTGGAG CAGTGAGATT ATTAGGCCTT CAGGGCCAGT GTCTCCATGC AGATCAGATG
961   GAGGCGGTGC TTGGCACATA CACCACCTCA CTGCCCATGC CCCCAGAAGT TGGTGCAGAT
1021  CATAAGGTGG CTTTTGGGGC TAATTGATTG AAGTTCCAAC ATAGTCTGTT TCTCCTAGGC
1081  TGGTAGCTGG CACCTTTGGC CCCATGTGTT TTTTAATTAT TTTTTCTTTT GAGACGAAAT
1141  CTCGCTCTAT CACCCAGGCT GAAGTGCAGT AGTGCAATCT CAGCTCACTG CAGCCTCTGC
1201  CTCCCGGGTT CAAGCAATTC TCCTGCCTCA GCCTCCCGAG TAGCCAGGAT TAAAGGTGCC
1261  TGCCACCACA CATGGCTAAT TTTTGTATTT TTAATAGAGA CGGGGTTTCA CCATGTTAGC
1321  CAGGCTGGTC TCAAACTCCT GACCTCAGGT GATCTTCCTG CCTCAGCCTC CCAAAGTGCT
1381  GGGATTACAG GTGTGAGCCA CTGCGCCCAG TCATGCCCAT GTGTTTTGGT GGTCTTGGCT
1441  GCTGATGGGT GGGGTGAGCC CCAGGAGGAA GTTGGGACAA GTCAACCTCA TGGCAGATGT
1501  GCCAGGGAGA GCTGCGGGTG AGATAGATTG TTCCTATCCC CCTCTCCTTG ATGTGGGAGG
1561  ACTCAGTACC TCCAGCACAC CCTTCTCATG GAGGTTGGTT ATGTGGTACT TGGCCTCAAG
1621  TGAACCAGCA CTTCATGAGT CCAGCTTTGT GCTAGACCAG CACTTGGGAT TGAGGGGGGC
1681  AGTGGCCACC CTCGGGGGAC CTTCTGACTC AGAGGACATG AGATGGCCAC ACTCGAGCAC
1741  TGTGTTCCTG ACCTTTCTGG GTCACAGGTC ACCTTGATGA TTGGATGAAA GTCTTAGATC
1801  TTCTTTCCAG AGAAAAGTCT ACAACATTCT ACTGAACCAG TCCAGAGGGT TCCCGGACCC
1861  CCGAAGCCCA CCCATGGGCT GGCTCTGGGA GGCAATGGCG CTGAGTATGG GGGCATCTCT
1921  CGCATGGATC CCCACAGATG GTACGGAGGG ATATCGGGCT GTCGGTGACG CACAGGTTCT
1981  CCACCAAGTC CTGGCTGTCG CAGGTCTGCC ACGTGTGCCA GAAGAGCATG ATATTTGGAG
2041  TGAAGTGCAA GCATTGCAGG TTGAAGTGTC ACAACAAATG TACCAAAGAA GCCCCTGCCT
2101  GTAGAATATC CTTCCTGCCA CTAACTCGGC TTCGGAGGAC AGAATCTGTC CCCTCGGACA
2161  TCAACAACCC GGTGGACAGA GCAGCCGAAC CCCATTTTGG AACCCTCCCC AAAGCACTGA
2221  CAAAGAAGGA GCACCCTCCG GCCATGAATC ACCTGGACTC CAGCAGCAAC CCTTCCTCCA
2281  CCACCTCCTC CACACCCTCC TCACCGGCGC CCTTCCCGAC ATCATCCAAC CCATCCAGCG
```

FIG. 12B-2

```
2341 CCACCACGCC CCCCAACCCC TCACCTGGCC AGCGGGACAG CAGGTTCAAC TTCCCAGCTG
2401 CCTACTTCAT TCATCATAGA CAGCAGTTTA TCTTTCCAGA CATTTCAGCC TTTGCACACG
2461 CAGCCCCGCT CCCTGAAGCT GCCGACGGTA CCCGGCTCGA TGACCAGCCG AAAGCAGATG
2521 TGTTGGAAGC TCACGAAGCG GAGGCTGAGG AGCCAGAGGC TGGCAAGTCA GAGGCAGAAG
2581 ACGATGAGGA CGAGGTGGAC GACTTGCCGA GCTCTCGCCG GCCCTGGCGG GGCCCCATCT
2641 CTCGCAAGGC CAGCCAGACC AGCGTGTACC TGCAGGAGTG GGACATCCCC TTCGAGCAGG
2701 TAGAGCTGGG CGAGCCCATC GGGCAGGGCC GCTGGGGCCG GGTGCACCGC GGCCGCTGGC
2761 ATGGCGAGGT GGCCATTCGC CTGCTGGAGA TGGACGGCCA CAACCAGGAC CACCTGAAGC
2821 TCTTCAAGAA AGAGGTGATG AACTACCGGC AGACGCGGCA TGAGAACGTG GTGCTCTTCA
2881 TGGGGGCCTG CATGAACCCG CCCCACCTGG CCATTATCAC CAGCTTCTGC AAGGGGCGGA
2941 CGTTGCACTC GTTTGTGAGG GACCCCAAGA CGTCTCTGGA CATCAACAAG ACGAGGCAAA
3001 TCGCTCAGGA GATCATCAAG GGCATGGGAT ATCTTCATGC CAAGGGCATC GTACACAAAG
3061 ATCTCAAATC TAAGAACGTC TTCTATGACA ACGGCAAGGT GGTCATCACA GACTTCGGGC
3121 TGTTTGGGAT CTCAGGCGTG GTCCGAGAGG GACGGCGTGA GAACCAGCTA AAGCTGTCCC
3181 ACGACTGGCT GTGCTATCTG GCCCCTGAGA TTGTACGCGA GATGACCCCC GGGAAGGACG
3241 AGGATCAGCT GCCATTCTCC AAAGCTGCTG ATGTCTATGC ATTTGGGACT GTTTGGTATG
3301 AGCTGCAAGC AAGAGACTGG CCCTTGAAGA ACCAGGCTGC AGAGGCATCC ATCTGGCAGA
3361 TTGGAAGCGG GGAAGGAATG AAGCGTGTCC TGACTTCTGT CAGCTTGGGG AAGGAAGTCA
3421 GTGAGATCCT GTCGGCCTGC TGGGCTTTCG ACCTGCAGGA GAGACCCAGC TTCAGCCTGC
3481 TGATGGACAT GCTGGAGAAA CTTCCCAAGC TGAACCGGCG GCTCTCCCAC CCTGGACACT
3541 TCTGGAAGTC AGCTGAGTTG TAGGCCTGGC TGCCTTGCAT GCACCAGGGG CTTTCTTCCT
3601 CCTAATCAAC AACTCAGCAC CGTGACTTCT GCTAAAATGC AAAATGAGAT GCGGGCACTA
3661 ACCCAGGGGA TGCCACCTCT GCTGCTCCAG TCGTCTCTCT CGAGGCTACT TCTTTTGCTT
3721 TGTTTTAAAA ACTGGCCCTC TGCCCTCTCC ACGTGGCCTG CATATGCCCA AG
```

FIG. 13A

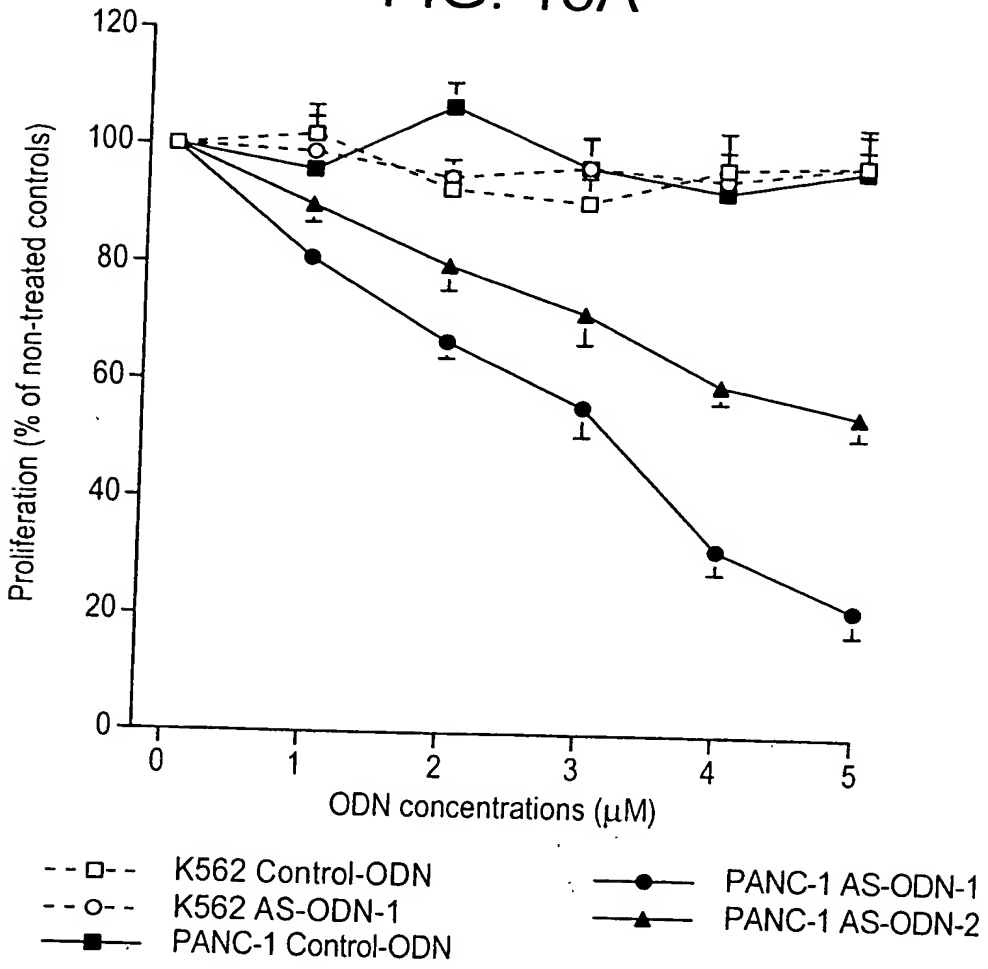


FIG. 13B

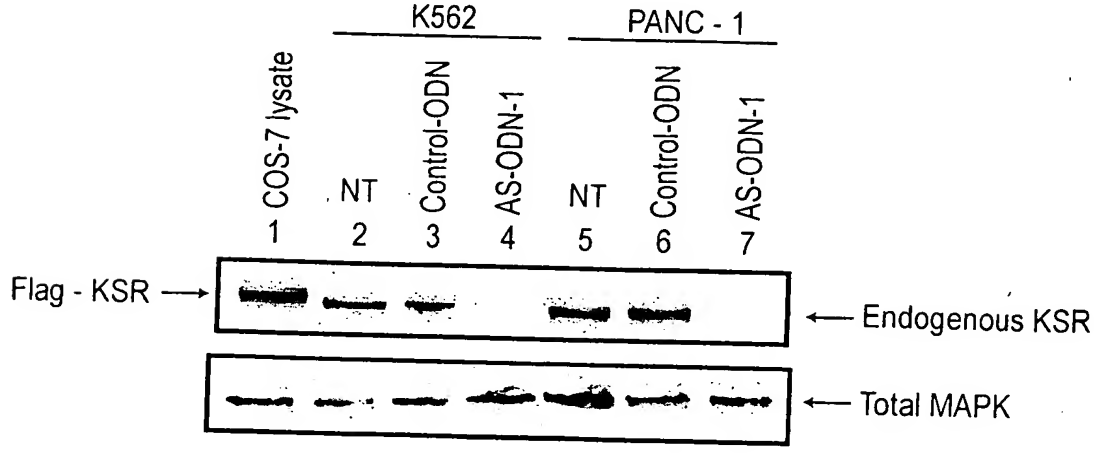


FIGURE 14

```
1     atgggagaga aggagggcgg tggcgggggg gatgcggcgg ccgcggaggg tggcgcaggg
60    gccgcggcca gccgggcgct gcagcagtgt gggcagctcc agaagctcat cgacatctcc
120   atcggcagtc tgcgcgggct gcgcaccaag tgcgcagtgt ctaacgacct cacccagcag
180   gagatacgga ccctagaggc aaagctggtc cgttacattt gtaagcagag gcagtgcaag
240   ctgagcgtgg ctcccggtga gaggacccca gagctcaaca gctacccccg cttcagcgac
300   tggctgtaca ctttcaacgt gaggccggag gtggtgcagg agatcccccg agacctcacg
360   ctggatgccc tgctggagat gaatgaggcc aaggtgaagg agacgctgcg gcgctgtggg
420   gccagcgggg atgagtgtgg ccgtctgcag tatgccctca cctgcctgcg gaaggtgaca
480   ggcctgggag gggagcacaa ggaggactcc agttggagtt cattggatgc gcggcgggaa
540   agtggctcag ggccttccac ggacaccctc tcagcagcca gcctgccctg gcccccaggg
600   agctcccagc tgggcagagc aggcaacagc gcccagggcc cacgctccat ctccgtgtca
660   gctctgcccg cctcagactc ccccaccccc agcttcagtg agggcctctc agacacctgt
720   attcccctgc acgccagcgg ccggctgacc ccccgtgccc tgcacagctt catcaccccg
780   cccaccacac cccagctgcg acggcacacc aagctgaagc caccacggac gccccccca
840   cccagccgca aggtcttcca gctgctgccc agcttcccca cactcacccg gagcaagtcc
900   catgagtctc agctggggaa ccgcattgat gacgtctcct cgatgaggtt tgatctctcg
960   catggatccc cacagatggt acggagggat atcgggctgt cggtgacgca caggttctcc
1020  accaagtcct ggctgtcgca ggtctgccac gtgtgccaga agagcatgat atttggagtg
1080  aagtgcaagc attgcaggtt gaagtgtcac aacaaatgta ccaaagaagc ccctgcctgt
1140  agaatatcct tcctgccact aactcggctt cggaggacag aatctgtccc ctcggacatc
1200  aacaacccgg tggacagagc agccgaaccc cattttggaa ccctccccaa agcactgaca
1260  aagaaggagc accctccggc catgaatcac ctggactcca gcagcaaccc ttcctccacc
1320  acctcctcca caccctcctc accggcgccc ttcccgacat catccaaccc atccagcgcc
1380  accacgcccc ccaacccctc acctggccag cgggacagca ggttcaactt cccagctgcc
1440  tacttcattc atcatagaca gcagtttatc tttccagaca tttcagcctt tgcacacgca
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1560  ttggaagctc acgaagcgga ggctgaggag ccagaggctg gcaagtcaga ggcagaagac
1620  gatgaggacg aggtggacga cttgccgagc tctcgccggc cctggcgggg ccccatctct
1680  cgcaaggcca gccagaccag cgtgtacctg caggagtggg acatcccctt cgagcaggta
1740  gagctgggcg agcccatcgg gcagggccgc tggggccggg tgcaccgcgg ccgctggcat
1800  ggcgaggtgg ccattcgcct gctggagatg gacggccaca accaggacca cctgaagctc
1860  ttcaagaaag aggtgatgaa ctaccggcag acgcggcatg agaacgtggt gctcttcatg
1920  ggggcctgca tgaacccgcc ccacctggcc attatcacca gcttctgcaa ggggcggacg
1980  ttgcactcgt ttgtgaggga ccccaagacg tctctggaca tcaacaagac gaggcaaatc
2040  gctcaggaga tcatcaaggg catgggatat cttcatgcca agggcatcgt acacaaagat
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2340  ctgcaagcaa gagactggcc cttgaagaac caggctgcag aggcatccat ctggcagatt
2400  ggaagcgggg aaggaatgaa gcgtgtcctg acttctgtca gcttggggaa ggaagtcagt
2460  gagatcctgt cggcctgctg ggctttcgac ctgcaggaga gacccagctt cagcctgctg
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2580  tggaagtcag ctgagttgta g
```
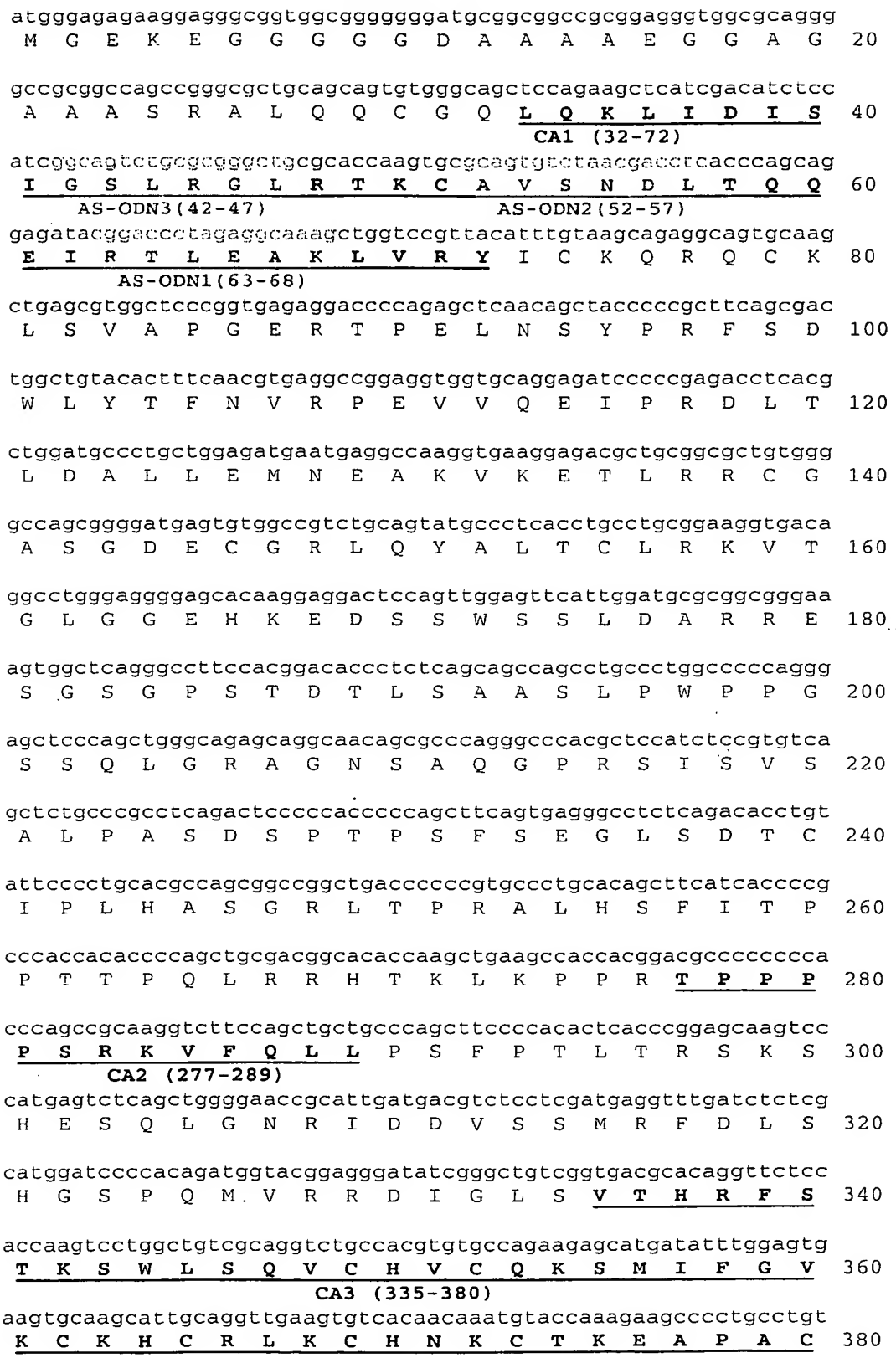

FIGURE 15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gccgcggccagccgggcgctgcagcagtgtgggcagctccagaagctcatcgacatctcc
A A A S R A L Q Q C G Q L Q K L I D I S 40
CA1 (32-72)
atcggcagtctgcgcgggctgcgcaccaagtgcgcagtgtctaacgacctcacccagcag
I G S L R G L R T K C A V S N D L T Q Q 60
AS-ODN3(42-47)
AS-ODN2(52-57)
gagatacggaccctagaggcaaagctggtccgttacatttgtaagcagaggcagtgcaag
E I R T L E A K L V R Y I C K Q R Q C K 80
AS-ODN1(63-68)
ctgagcgtggctcccggtgagaggaccccagagctcaacagctacccccgcttcagcgac
L S V A P G E R T P E L N S Y P R F S D 100
tggctgtacactttcaacgtgaggccggaggtggtgcaggagatcccccgagacctcacg
W L Y T F N V R P E V V Q E I P R D L T 120
ctggatgccctgctggagatgaatgaggccaaggtgaaggagacgctgcggcgctgtggg
L D A L L E M N E A K V K E T L R R C G 140
gccagcggggatgagtgtggccgtctgcagtatgccctcacctgcctgcggaaggtgaca
A S G D E C G R L Q Y A L T C L R K V T 160
ggcctgggaggggagcacaaggaggactccagttggagttcattggatgcgcggcgggaa
G L G G E H K E D S S W S S L D A R R E 180
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S S Q L G R A G N S A Q G P R S I S V S 220
gctctgcccgcctcagactcccccacccccagcttcagtgagggcctctcagacacctgt
A L P A S D S P T P S F S E G L S D T C 240
attcccctgcacgccagcggccggctgacccccgtgccctgcacagcttcatcaccccg
I P L H A S G R L T P R A L H S F I T P 260
cccaccacaccccagctgcgacggcacaccaagctgaagccaccacggacgccccccca
P T T P Q L R R H T K L K P P R T P P P 280
cccagccgcaaggtcttccagctgctgcccagcttccccacactcacccggagcaagtcc
P S R K V F Q L L P S F P T L T R S K S 300
CA2 (277-289)
catgagtctcagctggggaaccgcattgatgacgtctcctcgatgaggtttgatctctcg
H E S Q L G N R I D D V S S M R F D L S 320
catggatccccacagatggtacggagggatatcgggctgtcggtgacgcacaggttctcc
H G S P Q M V R R D I G L S V T H R F S 340
accaagtcctggctgtcgcaggtctgccacgtgtgccagaagagcatgatatttggagtg
T K S W L S Q V C H V C Q K S M I F G V 360
CA3 (335-380)
aagtgcaagcattgcaggttgaagtgtcacaacaaatgtaccaaagaagcccctgcctgt
K C K H C R L K C H N K C T K E A P A C 380

FIGURE 15 (cont'd)

```
agaatatccttcctgccactaactcggcttcggaggacagaatctgtcccctcggacatc
 R  I  S  F  L  P  L  T  R  L  R  R  T  E  S  V  P  S  D  I  400

aacaacccggtggacagagcagccgaaccccatttttggaaccctccccaaagcactgaca
 N  N  P  V  D  R  A  A  E  P  H  F  G  T  L  P  K  A  L  T  420

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 K  K  E  H  P  P  A  M  N  H  L  D  S  S  S  N  P  S  S  T  440

acctcctccacaccctcctcaccggcgcccttcccgacatcatccaacccatccagcgcc
 T  S  S  T  P  S  S  P  A  P  F  P  T  S  S  N  P  S  S  A  460

                    CA4 (432-498)
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 T  T  P  P  N  P  S  P  G  Q  R  D  S  R  F  N  F  P  A  A  480

tacttcattcatcatagacagcagtttatctttccagacatttcagcctttgcacacgca
 Y  F  I  H  H  R  Q  Q  F  I  F  P  D  I  S  A  F  A  H  A  500

gccccgctccctgaagctgccgacggtacccggctcgatgaccagccgaaagcagatgtg
 A  P  L  P  E  A  A  D  G  T  R  L  D  D  Q  P  K  A  D  V  520

ttggaagctcacgaagcggaggctgaggagccagaggctggcaagtcagaggcagaagac
 L  E  A  H  E  A  E  A  E  E  P  E  A  G  K  S  E  A  E  D  540

gatgaggacgaggtggacgacttgccgagctctcgccggccctggcggggccccatctct
 D  E  D  E  V  D  D  L  P  S  S  R  R  P  W  R  G  P  I  S  560

cgcaaggccagccagaccagcgtgtacctgcaggagtgggacatccccttcgagcaggta
 R  K  A  S  Q  T  S  V  Y  L  Q  E  W  D  I  P  F  E  Q  V  580

gagctgggcgagcccatcgggcagggccgctggggccgggtgcaccgcggccgctggcat
 E  L  G  E  P  I  G  Q  G  R  W  G  R  V  H  R  G  R  W  H  600

    CA5 (565-836, consisting of 11 conserved subdomains)
ggcgaggtggccattcgcctgctggagatggacggccacaaccaggaccacctgaagctc
 G  E  V  A  I  R  L  L  E  M  D  G  H  N  Q  D  H  L  K  L  620

ttcaagaaagaggtgatgaactaccggcagacgcggcatgagaacgtggtgctcttcatg
 F  K  K  E  V  M  N  Y  R  Q  T  R  H  E  N  V  V  L  F  M  640

ggggcctgcatgaacccgccccacctggccattatcaccagcttctgcaaggggcggacg
 G  A  C  M  N  P  P  H  L  A  I  I  T  S  F  C  K  G  R  T  660

ttgcactcgtttgtgagggaccccaagacgtctctggacatcaacaagacgaggcaaatc
 L  H  S  F  V  R  D  P  K  T  S  L  D  I  N  K  T  R  Q  I  680

gctcaggagatcatcaagggcatgggatatcttcatgccaagggcatcgtacacaaagat
 A  Q  E  I  I  K  G  M  G  Y  L  H  A  K  G  I  V  H  K  D  700

ctcaaatctaagaacgtcttctatgacaacggcaaggtggtcatcacagacttcgggctg
 L  K  S  K  N  V  F  Y  D  N  G  K  V  V  I  T  D  F  G  L  720

tttgggatctcaggcgtggtccgagagggacggcgtgagaaccagctaaagctgtcccac
 F  G  I  S  G  V  V  R  E  G  R  R  E  N  Q  L  K  L  S  H  740

gactggctgtgctatctggcccctgagattgtacgcgagatgacccccgggaaggacgag
 D  W  L  C  Y  L  A  P  E  I  V  R  E  M  T  P  G  K  D  E  760
```

FIGURE 15 (cont'd)

```
gatcagctgccattctccaaagctgctgatgtctatgcatttgggactgtttggtatgag
 D  Q  L  P  F  S  K  A  A  D  V  Y  A  F  G  T  V  W  Y  E   780

ctgcaagcaagagactggcccttgaagaaccaggctgcagaggcatccatctggcagatt
 L  Q  A  R  D  W  P  L  K  N  Q  A  A  E  A  S  I  W  Q  I   800

ggaagcggggaaggaatgaagcgtgtcctgacttctgtcagcttggggaaggaagtcagt
 G  S  G  E  G  M  K  R  V  L  T  S  V  S  L  G  K  E  V  S   820

gagatcctgtcggcctgctgggctttcgacctgcaggagagacccagcttcagcctgctg
 E  I  L  S  A  C  W  A  F  D  L  Q  E  R  P  S  F  S  L  L   840

atggacatgctggagaaacttcccaagctgaaccggcggctctcccaccctggacacttc
 M  D  M  L  E  K  L  P  K  L  N  R  R  L  S  H  P  G  H  F   860

tggaagtcagctgagttgtag
 W  K  S  A  E  L  -
```

FIGURE 16

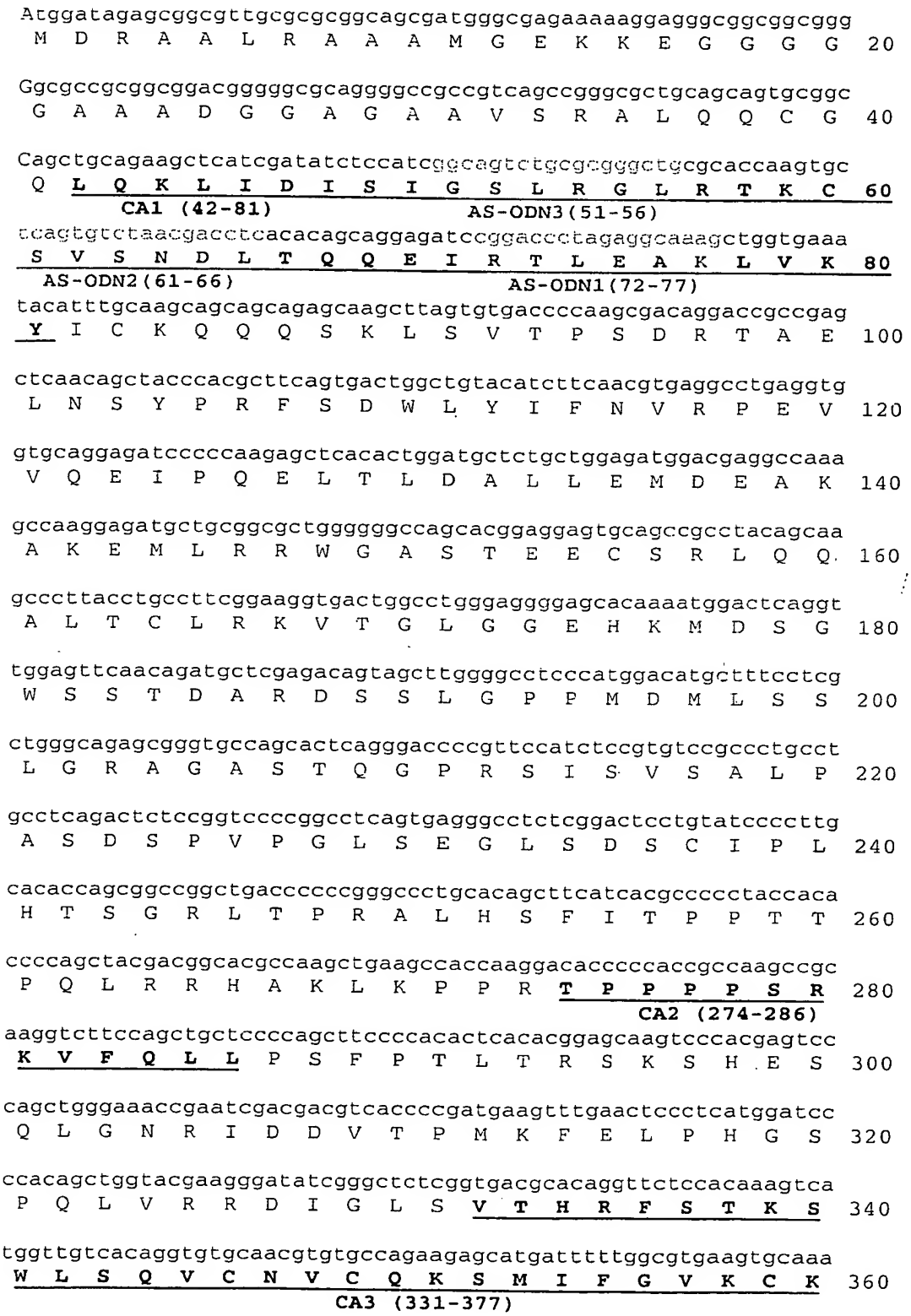

Atggatagagcggcgttgcgcgcggcagcgatgggcgagaaaaaggagggcggcggcggg
M D R A A L R A A A M G E K K E G G G G 20
Ggcgccgcggcggacgggggcgcaggggccgccgtcagccgggcgctgcagcagtgcggc
G A A A D G G A G A A V S R A L Q Q C G 40
Cagctgcagaagctcatcgatatctccatcggcagtctgcgcgggctgcgcaccaagtgc
Q L Q K L I D I S I G S L R G L R T K C 60
CA1 (42-81)
AS-ODN3(51-56)
tcagtgtctaacgacctcacacagcaggagatccggaccctagaggcaaagctggtgaaa
S V S N D L T Q Q E I R T L E A K L V K 80
AS-ODN2(61-66)
AS-ODN1(72-77)
tacatttgcaagcagcagcagagcaagcttagtgtgaccccaagcgacaggaccgccgag
Y I C K Q Q Q S K L S V T P S D R T A E 100
ctcaacagctacccacgcttcagtgactggctgtacatcttcaacgtgaggcctgaggtg
L N S Y P R F S D W L Y I F N V R P E V 120
gtgcaggagatcccccaagagctcacactggatgctctgctggagatggacgaggccaaa
V Q E I P Q E L T L D A L L E M D E A K 140
gccaaggagatgctgcggcgctgggggccagcacggaggagtgcagccgcctacagcaa
A K E M L R R W G A S T E E C S R L Q Q 160
gcccttacctgccttcggaaggtgactggcctgggaggggagcacaaaatggactcaggt
A L T C L R K V T G L G G E H K M D S G 180
tggagttcaacagatgctcgagacagtagcttggggcctcccatggacatgctttcctcg
W S S T D A R D S S L G P P M D M L S S 200
ctgggcagagcgggtgccagcactcagggaccccgttccatctccgtgtccgccctgcct
L G R A G A S T Q G P R S I S V S A L P 220
gcctcagactctccggtccccggcctcagtgagggcctctcggactcctgtatccccttg
A S D S P V P G L S E G L S D S C I P L 240
cacaccagcggccggctgacccccgggccctgcacagcttcatcacgccccctaccaca
H T S G R L T P R A L H S F I T P P T T 260
ccccagctacgacggcacgccaagctgaagccaccaaggacacccccaccgccaagccgc
P Q L R R H A K L K P P R T P P P P S R 280
CA2 (274-286)
aaggtcttccagctgctccccagcttccccacactcacacggagcaagtcccacgagtcc
K V F Q L L P S F P T L T R S K S H E S 300
cagctgggaaaccgaatcgacgacgtcaccccgatgaagtttgaactccctcatggatcc
Q L G N R I D D V T P M K F E L P H G S 320
ccacagctggtacgaagggatatcgggctctcggtgacgcacaggttctccacaaagtca
P Q L V R R D I G L S V T H R F S T K S 340
tggttgtcacaggtgtgcaacgtgtgccagaagagcatgatttttggcgtgaagtgcaaa
W L S Q V C N V C Q K S M I F G V K C K 360
CA3 (331-377)

FIGURE 16 (cont'd)

```
cactgcaggttaaaatgccataacaagtgcacaaaggaagctcccgcctgcaggatcacc
 H  C  R  L  K  C  H  N  K  C  T  K  E  A  P  A  C  R  I  T  380

ttcctcccactggccaggcttcggaggacagagtctgtcccgtcagatatcaacaaccca
 F  L  P  L  A  R  L  R  R  T  E  S  V  P  S  D  I  N  N  P  400

gtggacagagcagcagagccccattttggaacccttcccaaggccctgacaaagaaggag
 V  D  R  A  A  E  P  H  F  G  T  L  P  K  A  L  T  K  K  E  420

caccctccagccatgaacctggactccagcagcaacccatcctccaccacgtcctccaca
 H  P  P  A  M  N  L  D  S  S  S  N  P  S  S  T  T  S  S  T  440

ccctcatcgccggcacctttcctgacctcatctaatccctccagtgccaccacgcctccc
 P  S  S  P  A  P  F  L  T  S  S  N  P  S  S  A  T  T  P  P  460
                    CA4 (428-480)
aacccgtcacctggccagcgggacagcaggttcagcttcccagacatttcagcctgttct
 N  P  S  P  G  Q  R  D  S  R  F  S  F  P  D  I  S  A  C  S  480

caggcagccccgctgtccagcacagccgacagtacacggctcgacgaccagcccaaaaca
 Q  A  A  P  L  S  S  T  A  D  S  T  R  L  D  D  Q  P  K  T  500

gatgtgctaggtgttcacgaagcagaggctgaggagcctgaggctggcaagtcagaggca
 D  V  L  G  V  H  E  A  E  A  E  E  P  E  A  G  K  S  E  A  520

gaggatgacgaggaggatgaggtggacgacctccccagctcccgccggccctggaggggc
 E  D  D  E  E  D  E  V  D  D  L  P  S  S  R  R  P  W  R  G  540

cccatctctcgaaaggccagccagaccagcgtttacctgcaagagtgggacatcccctttt
 P  I  S  R  K  A  S  Q  T  S  V  Y  L  Q  E  W  D  I  P  F  560

gaacaggtggaactgggcgagcccattggacagggtcgctggggccgggtgcaccgaggc
 E  Q  V  E  L  G  E  P  I  G  Q  G  R  W  G  R  V  H  R  G  580
     CA5 (548-819, consisting of 11 conserved subdomains)
cgttggcatggcgaggtggccattcggctgctggagatggacggccacaatcaggaccac
 R  W  H  G  E  V  A  I  R  L  L  E  M  D  G  H  N  Q  D  H  600

ctgaagctgttcaagaaagaggtgatgaactaccggcagacgcggcatgagaacgtggtg
 L  K  L  F  K  K  E  V  M  N  Y  R  Q  T  R  H  E  N  V  V  620

ctcttcatgggggcctgcatgaacccacctcacctggccattatcaccagcttctgcaag
 L  F  M  G  A  C  M  N  P  P  H  L  A  I  I  T  S  F  C  K  640

gggcggacattgcattcattcgtgagggaccccaagacgtctctggacatcaataagact
 G  R  T  L  H  S  F  V  R  D  P  K  T  S  L  D  I  N  K  T  660

aggcagatcgcccaggagatcatcaagggcatgggttatcttcatgcaaaaggcatcgtg
 R  Q  I  A  Q  E  I  I  K  G  M  G  Y  L  H  A  K  G  I  V  680

cacaaggacctcaagtccaagaatgtcttctatgacaacggcaaagtggtcatcacagac
 H  K  D  L  K  S  K  N  V  F  Y  D  N  G  K  V  V  I  T  D  700

ttcgggctgtttgggatctcgggtgtggtccgagaggaacggcgcgagaaccaactgaaa
 F  G  L  F  G  I  S  G  V  V  R  E  E  R  R  E  N  Q  L  K  720

ctgtcacatgactggctgtgctacctggcccccgagatcgtacgagaaatgatcccgggg
 L  S  H  D  W  L  C  Y  L  A  P  E  I  V  R  E  M  I  P  G  740
```

FIGURE 16 (cont'd)

```
cgggacgaggaccagctgcccttctccaaagcagccgatgtctatgcattcgggactgtg
 R  D  E  D  Q  L  P  F  S  K  A  A  D  V  Y  A  F  G  T  V   760

tggtatgaactacaggcaagagactggccctttaagcaccagcctgctgaggccttgatc
 W  Y  E  L  Q  A  R  D  W  P  F  K  H  Q  P  A  E  A  L  I   780

tggcagattggaagtggggaaggagtacggcgcgtcctggcatccgtcagcctggggaag
 W  Q  I  G  S  G  E  G  V  R  R  V  L  A  S  V  S  L  G  K   800

gaagtcggcgagatcctgtctgcctgctgggctttcgatctgcaggagagacccagcttc
 E  V  G  E  I  L  S  A  C  W  A  F  D  L  Q  E  R  P  S  F   820

agcctgctgatggacatgctggagaggctgcccaagctgaaccggcggctctcccaccct
 S  L  L  M  D  M  L  E  R  L  P  K  L  N  R  R  L  S  H  P   840

gggcacttttggaagtcggctgacattaacagcagcaaagtcatgccccgctttgaaagg
 G  H  F  W  K  S  A  D  I  N  S  S  K  V  M  P  R  F  E  R   860

Tttggcctggggaccctggagtccggtaatccaaagatgtag
 F  G  L  G  T  L  E  S  G  N  P  K  M  -                     880
```

FIGURE 17

1 atgggagaga aggagggcgg tggcgggggg gatgcggcgg ccgcggaggg tggcgcaggg
AS-ODN4(1-18)
60 gccgcggcca gccgggcgct gcagcagtgt gggcagctcc agaagctcat cgacatctcc

120 atcggcagtc tgcgcgggct gcgcaccaag tgcgcagtgt ctaacgacct cacccagcag
AS-ODN3(124-141) AS-ODN2(154-171)
180 gagatacgga ccctagaggc aaagctggtc cgttacattt gtaagcagag gcagtgcaag
AS-ODN1(187-204) AS-ODN5(205-222)
240 ctgagcgtgg ctcccggtga gaggacccca gagctcaaca gctacccccg cttcagcgac
AS-ODN6(247-264)
300 tggctgtaca ctttcaacgt gaggccggag gtggtgcagg agatcccccg agacctcacg
AS-ODN7(298-315) AS-ODN8(321-338) AS-ODN9(351-368)
360 ctggatgccc tgctggagat gaatgaggcc aaggtgaagg agacgctgcg gcgctgtggg
AS-ODN10(379-396)
420 gccagcgggg atgagtgtgg ccgtctgcag tatgccctca cctgcctgcg gaaggtgaca

480 ggcctgggag gggagcacaa ggaggactcc agttggagtt cattggatgc gcggcgggaa
AS-ODN11(511-528) AS-ODN12
540 agtggctcag ggccttccac ggacaccctc tcagcagcca gcctgccctg gcccccaggg
(531-548)
600 agctcccagc tgggcagagc aggcaacagc gcccagggcc cacgctccat ctccgtgtca

660 gctctgcccg cctcagactc ccccaccccc agcttcagtg agggcctctc agacacctgt
720 attcccctgc acgccagcgg ccggctgacc ccccgtgccc tgcacagctt catcaccccg
780 cccaccacac cccagctgcg acggcacacc aagctgaagc caccacggac gccccccca
840 cccagccgca aggtcttcca gctgctgccc agcttcccca cactcacccg gagcaagtcc
900 catgagtctc agctggggaa ccgcattgat gacgtctcct cgatgaggtt tgatctctcg
960 catggatccc cacagatggt acggagggat atcgggctgt cggtgacgca caggttctcc
1020 accaagtcct ggctgtcgca ggtctgccac gtgtgccaga agagcatgat atttggagtg
1080 aagtgcaagc attgcaggtt gaagtgtcac aacaaatgta ccaaagaagc ccctgcctgt
1140 agaatatcct tcctgccact aactcggctt cggaggacag aatctgtccc ctcggacatc
1200 aacaacccgg tggacagagc agccgaaccc cattttggaa ccctccccaa agcactgaca
1260 aagaaggagc accctccggc catgaatcac ctggactcca gcagcaaccc ttcctccacc
1320 acctcctcca caccctcctc accggcgccc ttcccgacat catccaaccc atccagcgcc
1380 accacgcccc ccaacccctc acctggccag cgggacagca ggttcaactt cccagctgcc
1440 tacttcattc atcatagaca gcagtttatc tttccagaca tttcagcctt tgcacacgca
1500 gccccgctcc ctgaagctgc cgacggtacc cggctcgatg accagccgaa agcagatgtg
1560 ttggaagctc acgaagcgga ggctgaggag ccagaggctg gcaagtcaga ggcagaagac
1620 gatgaggacg aggtggacga cttgccgagc tctcgccggc cctggcgggg ccccatctct
1680 cgcaaggcca gccagaccag cgtgtacctg caggagtggg acatcccctt cgagcaggta
1740 gagctgggcg agcccatcgg gcagggccgc tggggccggg tgcaccgcgg ccgctggcat
1800 ggcgaggtgg ccattcgcct gctggagatg gacggccaca accaggacca cctgaagctc
1860 ttcaagaaag aggtgatgaa ctaccggcag acgcggcatg agaacgtggt gctcttcatg
1920 ggggcctgca tgaacccgcc ccacctggcc attatcacca gcttctgcaa ggggcggacg
1980 ttgcactcgt ttgtgaggga ccccaagacg tctctggaca tcaacaagac gaggcaaatc
2040 gctcaggaga tcatcaaggg catgggatat cttcatgcca agggcatcgt acacaaagat
2100 ctcaaatcta agaacgtctt ctatgacaac ggcaaggtgg tcatcacaga cttcgggctg
2160 tttgggatct caggcgtggt ccgagaggga cggcgtgaga accagctaaa gctgtcccac
2220 gactggctgt gctatctggc ccctgagatt gtacgcgaga tgacccccgg gaaggacgag
2280 gatcagctgc cattctccaa agctgctgat gtctatgcat ttgggactgt ttggtatgag
2340 ctgcaagcaa gagactggcc cttgaagaac caggctgcag aggcatccat ctggcagatt
2400 ggaagcgggg aaggaatgaa gcgtgtcctg acttctgtca gcttggggaa ggaagtcagt
2460 gagatcctgt cggcctgctg ggctttcgac ctgcaggaga gacccagctt cagcctgctg
2520 atggacatgc tggagaaact tcccaagctg aaccggcggc tctcccaccc tggacacttc
2580 tggaagtcag ctgagttgta g

FIGURE 18

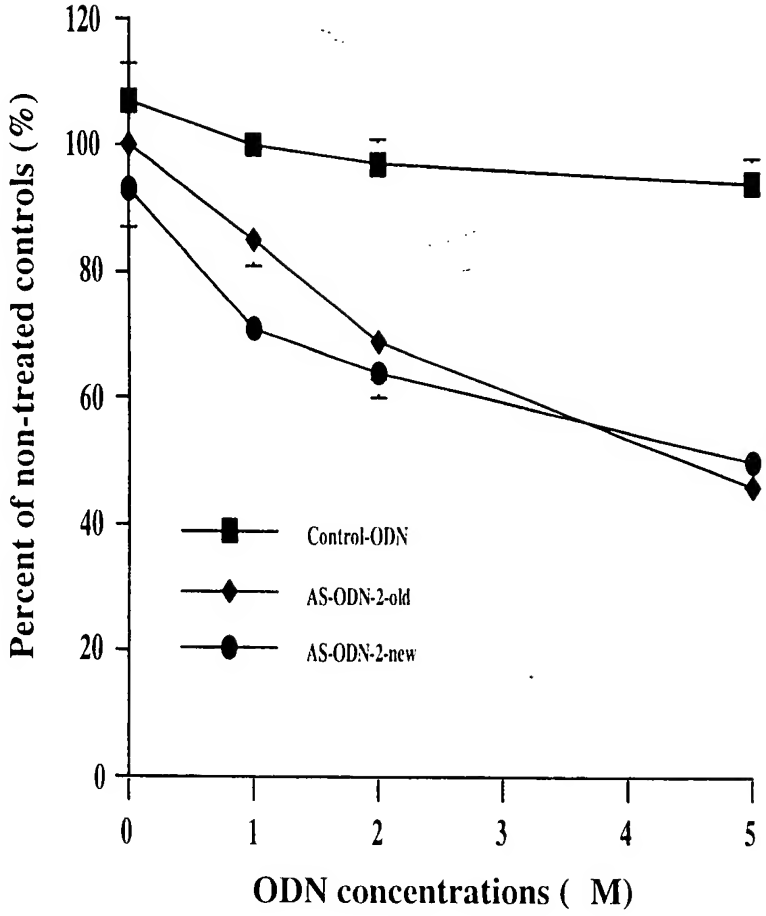
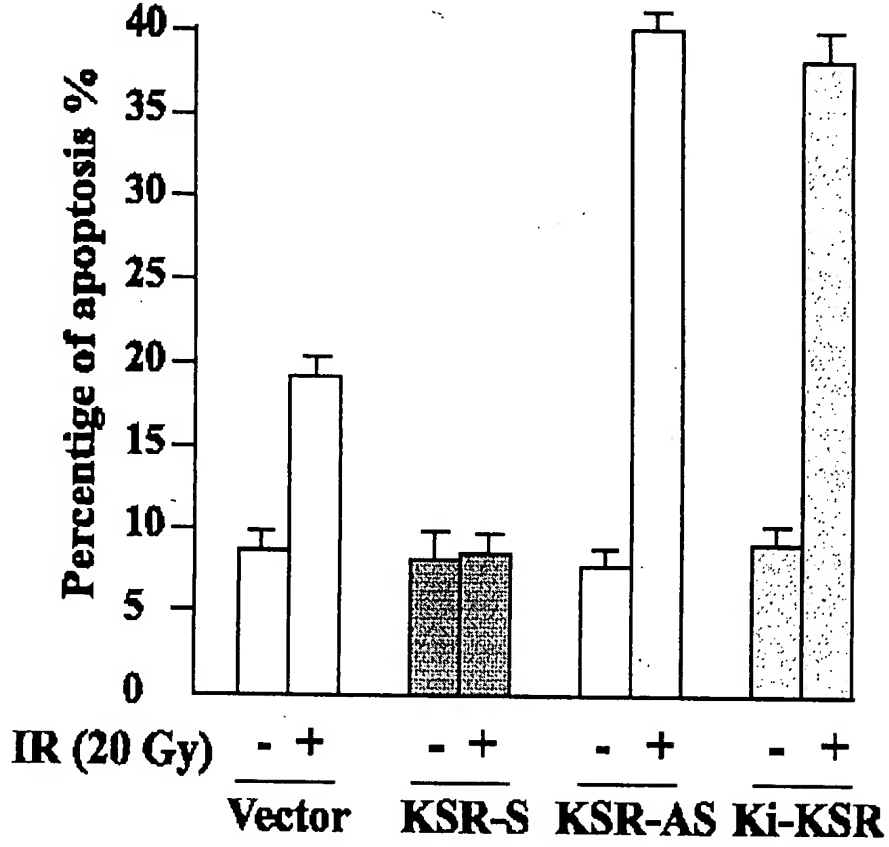


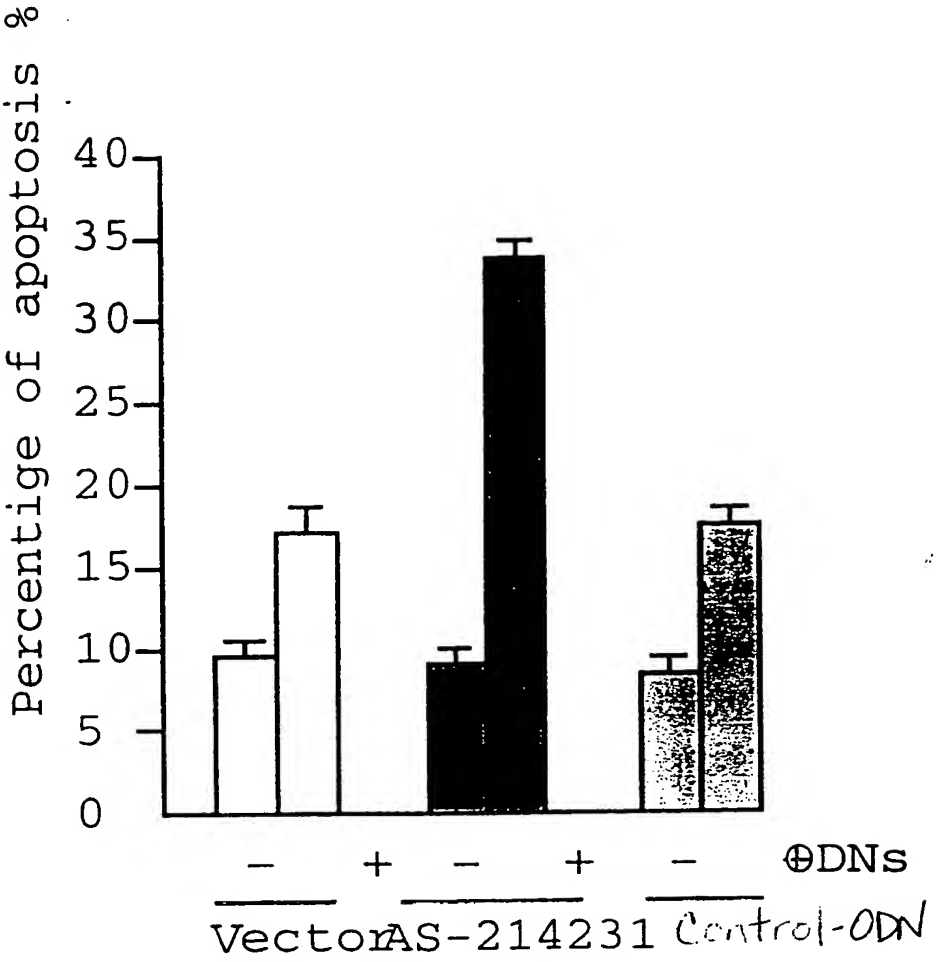
Figure 19. Proliferation assay of PANC-1 cells treated with old- and new- KSR AS-ODN2

FIGURE 19



Inactivation of KSR1 by KSR-AS sensitizes A431 cells to ionizing radiation-induced apoptosis

FIGURE 20


Percentige of apoptosis %
40
35
30
25
20
15
10
5
0
−
+
−
+
−
⊕DNs
Vector
AS-214231
Control-ODN